Haematology

Version 5.3

Corrected, Updated, Lighter

PLAB 1 Keys is for PLAB-1 and UKMLA-AKT (Based on the New MLA Content-Map)

With the Most Recent Recalls and the UK Guidelines

ATTENTION: This file will be updated online on our website frequently!

(example: Version 2.1 is more recent than Version 2, and so on)

Key 1	**Febrile Non-hemolytic Transfusion Reaction** (FNHTR)

√ ↑ in Body Temperature of around 1 to 2 °C during or after blood transfusion.

√ Occurs during transfusion or up to 4 hours after transfusion.

√ Can present with Chills/ Rigors **or** Asymptomatic with ↑ Temperature only.

√ **Rx**: (Paracetamol and Monitoring)

- Stop transfusion while continuing to give normal saline.
- Give Paracetamol.
- Resume the blood transfusion when the symptoms and fever subside.
- Observe the patient for 15-30 minutes

◙ **FNHTR "Febrile Non-Haemolytic Transfusion Reaction":**

- Fever of > 38
- ↑ in Temp. of at least 1 degree up to 2 degrees from pre-transfusion temperature.
- Other vitals are within normal with no significant changes from Pre-transfusion vitals.

Acute Hemolytic Transfusion Reaction (AHTR)

AHTR can be fatal. It starts **within minutes of transfusion.** Some S&S include:

√ Fever,

√ Hypotension/ Shock,

√ Pain at the transfusion site

± DIC (↑ Bleeding),

± Haemoglobinuria/ Hemoglobinemia,

± Feeling of impending doom "death".

Key 2

Leukemia Types

Chronic Myeloid Leukemia (CML)

- **40-50** YO.
- Massive Splenomegaly "May reach the right iliac fossa".

Remember (**CML = Crazy Massive Large Spleen**)

- ↑↑↑ WBCs "often > 100 X 10^9/L "
- Differential shows **Granulocytes** at ALL STAGES of development **without** Blast cells.

"↑ **Neutrophils** (Predominant), myelocytes, basophils, eosinophils"

- Cytogenetics → Ph Chromosome.

Chronic Lymphocytic Leukemia (CLL)

- Older (usually **> 65** YO).
- Asymptomatic or may present with **anemia** and **recurrent infections** (dysfunctional WBCs), **lymphadenopathy** …etc.
- ↑↑↑ WBCs (But dysfunctional) with **B Lymphocytes** Predominance.
- Blood smear → **Mature Lymphocytes with Smudge cells.**

Acute Lymphoblastic Leukemia (ALL)

- **Children.**
- **Pancytopenia:**

√ Low Hb → Anemia → *Fatigue*…etc.

√ Low WBCs → Recurrent *Infections*.

√ Lowe Platelets → Thrombocytopenia → *Bleeding*.

- Bone Marrow Aspiration/Biopsy → **Numerous Blasts**.

♦ In the exam, ***pancytopenia*** is either **ALL** or **Aplastic Anemia**. BM biopsy can differentiate.

Acute Myeloid Leukemia (AML)

Rarely Asked. However, remember these simple points:

- ADULT (Not children)
- Auer rods on blood film. • Adults. • Gingivitis. • Gum bleeding
- Bone Marrow Aspiration/Biopsy → **Numerous Blasts**.

If you see **numerous blast cells** on **Bone Marrow Biopsy and:**

♦ The patient is a **child** → **ALL** (Acute Lymphoblastic Leukemia)

♦ The patient is an **adult** → **AML** (Acute Myeloid Leukemia).

Numerous Blasts = Acute Leukemia.

Important Leukemia Clinchers: (The Age is Very Important)

ALL	Child (e.g. Up to 15 YO), **Pancytopenia**, **Blast cells**.
AML	Common in two age frames: 20-40 Years Old and Over 60 Years Old**,** **Auer rods**, **Blast cells**.
CML	Common in Middle age (40-50 YO) *but can occur in younger or older adults*, Massive Splenomegaly, **Philadelphia chromosome**, **Granulocytes** (Neutrophils, basophils eosinophils) **without blast cells, in all stages of maturation** (i.e. myelocytes, metamyelocytes…), Philadelphia chromos
CLL	Old (> 60 YO), Typically, there is no or mild splenomegaly, but it can be present in some cases., **smudge cells**, **Cervical Lymphadenopathy**, **Mature Lymphocytes**.

Example **(1),**

44 YO male presents with fatigue and otherwise asymptomatic.

Hb: 81 g/L ▌WBCs: 133 X 10^9/L ▌Platelets: 550 X 10^9/L.

↑ Neutrophils, basophils, eosinophils.

Peripheral blood smear shows → all stages of maturation.

The likely Diagnosis → **CML "Chronic Myeloid Leukemia"**.

Note that the patient does not always have massive splenomegaly.

The presence of **all stages of maturation** along with the **enormous increase in the WBCs** diagnose CML.

Example **(2),**

5 YO child presents with fever and pallor. He is not active and always feels tired. His spleen is enlarged. His labs:

Hb: 72 g/L ▌WBCs: 2 X 10^9/L ▌Platelets: 44 X 10^9/L.

The likely Diagnosis → **ALL "Acute Lymphocytic Anemia"**.

Important Notes:

√ Note that **WBCs** in **ALL** might be **normal**, **high** or **low**.

√ The symptoms of **pallor** and **fatigue** are attributed to the **Anemia** and these are the most common presenting features in ALL.

√ **Fever** is due to recurrent **infections** because **WBCs** are **low**.

√ Note that **Bone morrow** should be performed next as it will show **Blast Cells** and thus confirm the diagnosis.

Example **(3),**

29 YO male with fatigue, loss of energy, ecchymosis, gum bleeding, Dizziness, Dyspnea on exertion, Bone pain and Hepatosplenomegaly.

WBCs os 102 X 10^9/L. Bone Marrow Biopsy → Numerous Blasts.

The likely Dx → **AML "Acute Myeloid Leukemia"**.

If you see **numerous blast cells** on **Bone Marrow Biopsy and:**

♦ The patient is a **child** → **ALL** (Acute Lymphoblastic Leukemia)

♦ The patient is an **adult** → **AML** (Acute Myeloid Leukemia).

Numerous Blasts = Acute Leukemia.

Example **(4),**

51 YO ♀ presents for check-up. Pale Conjunctivae are noted. Upon examination, there is massively enlarged spleen. The FBC results are:

Hb: 102 g/L ▌WBCs: 65 X 10^9/L ▌Platelets: 802 X 10^9/L.

The likely Dx → **CML "Chronic Myeloid Leukemia"**

√ **CML** → **C**razy **M**assive **L**arge spleen.

√ Age is also supportive (40-50)

√ Very High WBCs "Normal WBC: 4-11 X 10^9/L

Example **(5),**

A 4 YO child presents with fever, pallor, tiredness and decreased appetite. There are deep cervical palpable LNs but not tender. There is splenomegaly. There is a Hx of recurrent throat infections.

Hb 9 ▌MCV 80 ▌WBCs 2

The likely Dx → **Acute Lymphoblastic Leukemia (ALL).**

Example **(6),**

50 YO ♂, Malaise and Tiredness, Splenomegaly reaching right iliac fossa, No lymphadenopathy.

The likely cell type on a blood smear → **Granulocytes WITHOUT Blast cells**

√ This is likely CML (Chronic Myeloid Leukemia).

√ Remember: **CML** → **C**razy **M**assive **L**arge spleen.

√ In CML, Blood smear will show **Granulocytes** at all stages of maturation.

√ There **won't be Blast cells**. Remember, Blast cells are seen in ACUTE Leukemias, not chronic.

√ Another hint towards CML is the age (40-50 YO).

◙ In PLAB, **Massive Splenomegaly** is either **CML** or **Malaria**.

Malaria would have a Hx of travelling.

Example **(7),**

15 YO girl presents with chest infection which was treated. A few days later, the girl returns with another chest infection. Upon looking at her Lab results, you find that there is always mild anemia and thrombocytopenia.

The likely Dx → **Acute Lymphoblastic Leukemia (ALL)**.

√ Anemia (**low Hb**)

√ Thrombocytopenia (**low Platelets**)

√ Recurrent Infections (i.e. **low WBCs**)

→ **Pancytopenia**.

Pancytopenia in PLAB 1 is usually either **ALL** or **Aplastic Anemia**.

She is young age and no other sign of aplastic anemia → **ALL**

Example **(8),**

73 YO ♂ presents with enlarged cervical LNs, Weakness, Pale conjunctiva and Recurrent infections.

The likely cell type to be found on a blood smear → **Mature Lymphocytes**.

√ The likely Dx here is → Chronic Lymphocytic Leukemia (CLL)

√ Although there would usually be ↑ WBCs, they are non-functioning → recurrent infections.

√ **He is old age (>65) + features of Leukemia → CLL**

√ Remember that **CML** occurs in age (40-50) + often Massive Splenomegaly.

√ Remember that in **CML**, Blood smear → **Granulocytes WithOut Blast cells**.

√ In CLL, Blood smear → **Mature Lymphocytes with Smudge cells.**

Example **(9),**

A 5 YO boy is brought by his mother to the ED with bleeding from his gums and nose and recurrent sore throats. He has pale conjunctivae.

→ The likely cell type to be found → **Blast Cells**.

√ Pale conjunctivae → Anemia (**Low Hb**)

√ Bleeding → **low platelets**

√ Recurrent infections → **Low WBCs**

Pancytopenia + a **Child** → **Acute Lymphoblastic Leukemia** (ALL) → **Blasts**

◙ Next step → **Bone marrow biopsy**.

Key 3

Lymphoma

Lymphadenopathy + Splenomegaly + Weight loss ± B Symptoms

→ Think of **Lymphoma** (either Hodgkin or Non-Hodgkin).

♦ **Hodgkin** →

√ Histology shows **Reed-Sternberg cells "important √"**

= "Multinucleated Giant Cells".

√ Bimodal Age: **< 25 or > 55**.

♦ **Non-Hodgkin** → No Reed-Sternberg cells. Age is usually **25-40** YO.

♦ **B Symptoms** →

Unintended Weight Loss ▌Unexplained Fever ▌Drenching Night Sweats.

Manifestations of Lymphoma

√ **Painless**, **Rubbery** slowly progressive Peripheral **lymphadenopathy**. "**The commonest**".

√ Systemic manifestations → fever, malaise, **fatigue**, **weight loss** (Late stage).

√ **B Symptoms** → **Unintended Weight Loss ▌Unexplained Fever ▌Night Sweats**

√ **Splenomegaly**, **Hepatomegaly**.

√ BM is frequently involved → **Pancytopenia** → Anemia, Infections, Bleeding.

√ **Excisional biopsy** is essential.

♦ Important Notes:

• The most common presentation of Hodgkin's lymphoma is **painless**, **firm lymphadenopathy** in one or two areas (supraclavicular/ cervical LNs).

• Remember that constitutional symptoms such as fever, night sweats and weight loss present in **only 33%** of the patients.

• **Excisional biopsy** is essential for the diagnosis.

• Also remember that Hodgkin's lymphoma has bimodal age presentation: **<25** YO or **> 55 YO**.

A Quick Note

Some students might get confused with the **Hemoglobin Units**.

Simply, 13 g/**dL**. Is the same as 130 g/**L**, and so on.

Example (1),

19 YO ♂ presents with a painless neck lump that is enlarging in size. He says that he has been told that he is getting thinner. He also says that he feels tired, fatigued and suffers from night sweats. He denies any recent Hx of travel abroad. His spleen is enlarged and his temperature is 38.3.

The likely Dx → **Hodgkin's Lymphoma**.

Painless Cervical Lymphadenopathy + B Symptoms ± Splenomegaly

→ **Think of Lymphoma**

Giving his age is < 25, it is likely Hodgkin's.

Remember, Hodgkin's lymphoma has bimodal age:

Either <25 YO

Or > 55 YO

In PLAB 1, it is unlikely that you will need to differentiate between Hodgkin and Non-Hodgkin's lymphoma. They will usually give you either one, pick it if the Triad above exists.

Example (2),

26 YO ♀ Has returned from New York City to the UK. 3 weeks later, she presents with Drenching night sweats and fever. O/E: Enlarged, non-tender cervical LNs.

The Likely Diagnosis → **Lymphoma**.

- Do not get tricked by the Hx of travel. New York is not a prone area for TB.
- TB "Tuberculosis" prone areas include → **South Asia**, **Sub-Saharan Africa**.

♦ **Painless Cervical Lymphadenopathy + B Symptoms** ± Splenomegaly

→ **Think of Lymphoma**

♦ **B Symptoms →**

Unintended Weight Loss ▌Unexplained Fever ▌Drenching Night Sweats.

• **Points in favour of TB:**

√ Hx of travel to or from South Asia or Sub-Saharan Africa.

√ the Palpable LNs are initially tender, firm and discrete.

√ There is usually Chronic Productive Cough ± Bloodstained sputum.

√ ± Erythema Nodosum = (Painful nodules usually on the shins of legs).

◙ **Risk Factors of TB**

→ **Homeless / Drug Abuser / Smoker / Low Socioeconomic class.**

◙ Although **Toxoplasmosis** can present with Splenomegaly and cervical lymphadenopathy, **weight loss** is usually **not** seen in Toxoplasmosis.

Example (3),

56 YO ♂ with HIV- infection presents with painless peripheral lymphadenopathy, night sweats, weight loss, fever and splenomegaly.

The likely Dx → **Non-Hodgkin's Lymphoma**.

Important note

The most common **HIV-related lymphomas** is diffuse large B-cell **non-Hodgkin's lymphoma**, followed by Burkitt's lymphoma.

◙ **The Diagnostic Test in Lymphoma** → **LN Biopsy**

Key 4

Disseminated Intravascular Coagulopathy (DIC)

Sepsis + **Bleeding**

"e.g., Purpura, Petechia, GIT bleeding, Ecchymosis, ENT bleeding, Bleeding from the sites of venepuncture"

+

↓ **Platelets**, ↓ **Fibrinogen**

↑ **PT**, ↑ **PTT**, ↑ **INR**, ↑ Fibrin degradation products e.g., **D-dimers**

→ **DIC "Disseminated Intravascular Coagulation".**

♦ **Disseminated intravascular coagulation** (**DIC**) is a condition in which blood clots form throughout the body, blocking small blood vessels. Symptoms may include chest pain, shortness of breath, leg pain, problems speaking, or problems moving parts of the body. As clotting factors and platelets are used up "depleted", bleeding may occur.

♦ **Features**

→ **Bleeding from any site**. This may include blood in the urine, blood in the stool, or bleeding into the skin, purpura, petechia, ecchymosis, GIT bleeding, ENT bleeding (epistaxis), bleeding from venepuncture sites.

• Complications may include organ failure.

♦ **Common causes**

→ **Sepsis (eg, after infection: pneumonia)** is one of the most frequent causes of DIC. (You may find ↑ WBC, ↑CPR, ↑Temperature, Tachycardia).

Other causes may include: surgery, major trauma, cancer, and complications of pregnancy. (Any of these can precipitate DIC).

♦ **Diagnosis** is typically based on blood tests. Findings may include:

low platelets, **low fibrinogen**,

high INR, **high PT**, **high PTT**, **high D-dimer**, **high bleeding time.**

♦ **Treatment**

√ Treat the underlying condition (e.g., **sepsis**).

√ Platelet or **Fresh Frozen Plasma** (FFP) transfusion.

PT: **Prothrombin Time** (Normal: 10-14).

PTT: activated **Partial Thromboplastin Time** (Normal: 35-45).

Important Haematology Clinchers

• **↑ PTT +** (Bleeding into muscles or joints or easily bleeds)

→ think of **Haemophilia**. (*isolated ↑ in PTT*)

• **↑ PTT and ↑ Bleeding Time +** (Mucosal Bleeding)

→ think of **VWD (Von Willebrand Disease)**.

• **↑ PTT and ↑ PT and ↑ Bleeding Time and ↓ Platelets +** (Bleeding at any site e.g., purpura, petechia, GIT, ENT, venepuncture site)

→ think of **DIC (Disseminated Intravascular Coagulopathy)**.

	• Only ↓ **Platelets** + Bleeding/ Purpura ± History of URTI → **ITP (Idiopathic Thrombocytopenic Purpura)**. **PT** = Prothrombin Time (Normal: 10-14) ▌**PTT** = activated Partial Thromboplastin Time (35-45).
Key 5	**Polycythemia Rubra Vera (PRV)** √ **Fatigue**, **Tiredness**, **Lethargy** (+) √ **Pruritus** "itching" especially **after hot shower** (+) √ **Splenomegaly** (+) √ **Burning sensations in fingers and toes** (+) √ **Gout** "due to ↑ cell turnover" → **Polycythemia Rubra Vera** (PRV) "= **Primary Polycythemia**" • It is a **malignancy**. • Mutation in **JAK2** gene → **JAK Mutation Screen is the Investigation of Choice**. → **Excessive Proliferation** of **RBCs**, **WBCs** and **Platelets** (**All ↑**) → High "Hematocrit": may exceed 55% → **Hyperviscosity** of the blood → ↑ Risk for **MI**, **DVT**, **PE**, Stroke.

- **Other manifestations:**

√ Facial Plethora "redness".

√ **Headache**

√ Hepatomegaly/ Splenomegaly

√ **Low/normal** serum erythropoietin.

[Note: In **Secondary** Polycythemia → **Erythropoietin** is **High**].

- **Treatment:**

√ **Venesection** "**Phlebotomy**" → to reduce the elevated haematocrit and thus reduce the blood viscosity "the **mainstay** step of the treatment".

√ Low dose **Aspirin** (**75 mg OD**) → for fear of thrombosis.

√ It is a malignancy

→ **Chemotherapy**:

< 40 YO → Interferon ▌40 YO → Hydroxyurea.

Secondary Polycythemia = Secondary Erythrocytosis

♦ Remember in **Polycythemia Rubra Vera "PRV" (Primary Polycythemia), all 3 lines: Hemoglobin, WBCs and Platelets are Elevated**.

♦ In **Secondary Polycythemia**, **Only Hemoglobin is Elevated**.

♠ One **important cause** of 2ry Polycythemia to remember is **Chronic Hypoxia** (such as those who are **chronic smokers → COPD**).

Other causes → High Altitudes/ Cyanotic Congenital Heart diseases.

♠ Chronic Hypoxia → Stimulates the **kidneys** to produce more and more **Erythropoietin** → Which stimulates the bone Marrow to produce → More and more RBCs so they can carry more O2 to the tissues.

Important note

√ In **Primary** Polycythemia (PRV) → **Erythropoietin** is either **Low** or **Normal**.

√ In **Secondary** Polycythemia → **Erythropoietin** is **High**.

Key 6

Glucose-6-Phosphate-Dehydrogenadse (G6PD) Deficiency

◙ ↓ G6PD enzyme → ↓ Glutathione → RBCs become vulnerable to oxidative damage → **Hemolysis**.

◙ Exposure to precipitating factors such as certain drugs "e.g. **anti-malarial Primaquine**", **Fava beans**, **Infection**

→ *Severe Hemolysis*

→ *Jaundice, Red or Dark Urine, Back and Abdominal pain.*

◙ Important Triggers [useful in the exam]:

Fava Beans ▌Anti-malarial drugs ▌Sulfa drugs ▌Infections (e.g. UTIs)

◙ Important hints towards G6PD Deficiency in the exam:

√ **Male** (as the disease is X-linked Recessive)

√ **African** or **Mediterranean**.

√ **Heinz Bodies** or **Bite Cells**.

√ **Recent infection** or recent ingestion of **drugs** or **fava beans**.

√ Hx of **Neonatal Jaundice**.

√ Presents with one or more of: Jaundice, Dark urine, Back and Abdominal pain.

◙ The definitive Diagnostic Test

→ **G6PD enzyme activity** (6 weeks after the hemolytic attack).

◙ Treatment:

• ***Avoid Triggers.*** • ***IV fluids.*** • ***If severe Haemolysis → Blood Transfusion.***

	Pay Attention! **Sometimes the question won't have G6PD deficiency in the options. Instead, pick (Hemolytic Anemia).**
Key 7	**What test is used in cross-matching "Blood Transfusion Preparation"?** **Answer → Indirect Coomb Test (Indirect Anti-Globulin Test)** **◙ Direct Coomb Test (Direct Anti-globulin test):** √ It detects antibodies on the **RBCs Surfaces**. √ Used for → **Autoimmune Haemolytic Anemia** (AHA). **◙ Indirect Coomb Test (Indirect Anti-globulin test):** √ It detects antibodies in the **Serum**. √ 2 Major uses: • **Blood Transfusion Preparation** (**Cross-matching**). • **Antenatal antibody screening** → Screening a pregnant ♀ for **IgG** antibodies that can cross the placenta and cause hemolysis in fetal blood.

	◙ **Osmotic Fragility test** → Hereditary Spherocytosis.
Key 8	**Multiple Myeloma (MM)** √ It is a cancer of **Plasma Cells**. √ "Overgrowth of plasma cells replacing the bone marrow tissues" + Overproduction of Non-functioning Igs (Immunoglobulins). **√ The main presenting Symptoms:** • **Bone pain** "Particularly in the **back** and **ribs**". • **Hypercalcemia** → **Polyuria**, **Polydipsia**, Low mood, **Confusion**. • **Anemia** → **Fatigue**, **Weakness**, **lethargy**, Pallor, Dyspnea on exertion. **√ Others:** • **Recurrent Infections** → As the immunoglobulins are functionless. • **Renal Failure**. √ **So, you may find** **Low** hemoglobin, **high** serum urea and creatinine, **high** serum calcium. **Bone pain** + **Anemia** + **Renal failure** → Think: **Multiple Myeloma**

√ Important Notes on Investigations of Multiple Myeloma:

♦ **Bone Marrow Biopsy** → **Abundant Plasma cells** (**Diagnostic √**).

♦ **Serum Protein Electrophoresis** → **↑↑ Monoclonal Immunoglobulin Spike**.

♦ **Urine Protein Electrophoresis** → **Bence Jone's Protein**. √

♦ **Blood Film** → **Rouleaux Formation**.

♦ **X-Ray Skeleton** → **Lytic Lesions** "plasma cells → Osteoclasts → Bone Lysis".

♦ **↑ Ca^{++}** (>2.6 mmol/L) but with **Normal Alkaline Phosphatase** (30-150 U/L).

♦ **Anemia** (**Normocytic Normochromic**).

♦ **Renal functions could be impaired** (Low GFR, High Urea and Creatinine).

♦ **High ESR.**

Important: **Don't mix things up**. Plasma cells are cells seen on BM biopsy whereas Bence Jone's is Protein seen on urine protein electrophoresis!

Example **(1),**

60 YO ♂ presents with Hx of Back and Ribs pain + being Thirsty + Tiredness.

Hb is 90 g/L (low) ▌Ca^{++} is 4 (high) ▌ALP is 115 (normal) ▌ESR is 88 ▌eGFR is 45 (low).

◙ The likely Dx → **Multiple Myeloma**.

◙ The cell type to be found in BM → **Plasma Cells**.

◙ The Diagnostic Test → **Bone Marrow Biopsy**.

◙ The likely finding on blood film → **Rouleaux Formation**.

√ Anemia is the commonest laboratory finding in MM.

√ Renal Impairment presents in 50% of MM cases.

√ In MM, High Calcium but normal ALP.

Example **(2),**

92 YO ♀ complains of severe back pain. She claims that she had a fight and someone has broken her back and insists that her mother is coming to visit her at the hospital.

Hb 109 (low) ▌Urea 7.5 (high) ▌Creatinine 285 (high) ▌Calcium 3 (high)

◙ The likely Dx → **Multiple Myeloma**.

◙ The cell type to be found in **BM** → **Plasma Cells**.

◙ The protein to be found on **Urine Electrophoresis** → **Bence-Jones Protein**

√ The features present in this stem supporting the Dx of Multiple Myeloma:

Back pain ▌Confusion "her mother is visiting her" ▌

Anemia ▌Hypercalcemia ▌Impaired Renal Function

Example (3),

A 57-year-old man presents with lethargy and he looks pale. Blood pressure is 150/100.

Urinalysis: Blood +++, Protein +++, Creatinine: Elevated, Calcium is high

Other tests are normal.

What's the appropriate investigation among the following options?

a. **Urine for Bence Jones protein**

b. Renal Ultrasound

c. Cystoscopy

d. Blood culture

e. 24hour urine collection

Pale and lethargy → Anemia

Renal Failure

Hypercalcemia

Others (not mentioned here): Bone pain, Recurrent infection

Think → **Multiple Myeloma**

	◙ Urine electrophoresis → **Bence Jones Protein.** ◙ The cell type to be found in BM → **Plasma Cells**. ◙ The Diagnostic Test → **Bone Marrow Biopsy**. ◙ The likely finding on blood film → **Rouleaux Formation.**
Key 9	A patient present with **Pancytopenia** (Low Hb, Low WBCs, Low Platelets). What is **the diagnosing test**? → **Bone Marrow Biopsy** **Some Important Differentials for Pancytopenia:** **√** Acute Lymphocytic Leukemia → Numerous Blasts. **√** Aplastic Anemia → Hypoplastic bone marrow. (Reduction in hemopoietic cells)
Key 10	◙ **In PLAB 1, if you see a patient presenting with hypercalcemia** **(e.g. ↑ Thirst "Polydipsia", Polyuria, bone pain, confusion, low mood)** Think of: • Bone metastasis "e.g. from prostate, breast". • SCC of the lung. • Multiple Myeloma. (ALP is normal) • Primary Hyperparathyroidism (associated ↑ PTH, ↓ Phosphate).

	◙ **Hypercalcemia picture:** • Neuro → lethargy, Confusion, Depression. • GIT → Constipation. • Renal → polyuria (increased urination), Polydipsia (Thirst). • CVS → ECG: Short QT interval
Key 11	**Low Hb**, **Low MCV**, **Low Ferritin**, **low transferrin saturation** **High TIBC (total iron binding capacity)** **High RDW** (red cell distribution width) → **Iron Deficiency Anemia** **Other features of IDA:** √ **Angular Stomatitis** (can also occur with Vit B12 def., look at MCV). √ **Red sore tongue** √ **Koilonychia** **Causes of IDA:** ◙ The most common cause → GIT Blood Loss → e.g., NSAIDs use, Colorectal Carcinoma, Gastric Carcinoma, Gastric or Duodenal Ulcer. ◙ The most common cause in premenopausal ♀ → Menorrhagia.

◙ Other causes:

- Dietary inadequacy.
- ↑ iron requirements → Pregnancy.
- Malabsorption → e.g., Celiac disease.

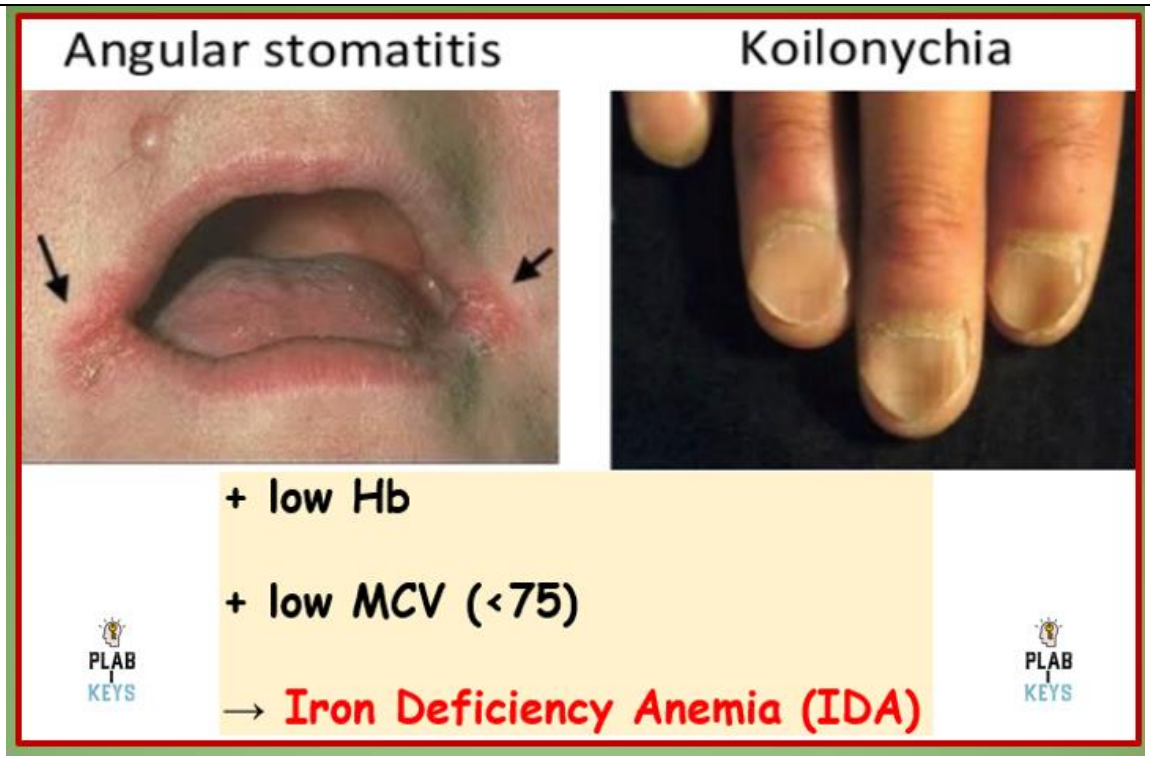
Treatment:

√ Treat the underlying cause.

√ Iron supplements (e.g., ferrous sulphate).

When is Blood Transfusion indicated?

- If Hb **< 7** (either symptomatic or not).
- If Hb **< 8** + there are symptoms of anemia (eg, fatigue, tachycardia, pallor).
- If Hb **< 9** + there is a known cardiovascular disease.



Example (1),

An old lady with Rheumatoid Arthritis (RA) is on Methotrexate and Naproxen found to have anemia (low Hb and low MCV).

The likely cause → **Chronic GIT Blood Loss**

(due to prolonged use of **NSAIDs** -**Naproxen**-) → The commonest cause for **Iron Deficiency Anemia**

Note, **Methotrexate** can cause **Folate Deficiency** and thus Macrocytic Anemia; however, in this example, low MCV is suggestive of GIT bleeding due to NSAIDs intake for a long period of time for RA.

Example (2),

An old lady with Rheumatoid Arthritis (RA) is on Methotrexate and Naproxen found to have anemia (low Hb and <u>High</u> MCV).

The likely cause for her anemia → **Methotrexate**.

√ As **MCV** is high (**Macrocytic**) → either **Vitamin B12** or **Folic Acid deficiency**.

√ **Methotrexate** can cause **Folate Deficiency**.

Example (3),

An old lady with Rheumatoid Arthritis (RA) is on Methotrexate found to have anemia (low Hb and <u>low</u> MCV).

What is the likely cause for her anemia among the following options?

A) Menorrhagia.
B) **Anemia of chronic disease**.
C) Vitamin B12 deficiency.
D) Folate deficiency.

√ No Hx of menorrhagia is mentioned. Plus, she is old, and likely postmenopausal.

√ Both Vitamin B12 and Folate deficiency have Macrocytic anemia (high MCV), here, it is low. Although methotrexate is anti-folic acid, the MCV here is low.

√ Although **Anemia of chronic disease** is usually Normochromic Normocytic, it **can be** hypochromic microcytic such as in the cases of Rheumatoid Arthritis and Crohn's disease.

Example (4),

A woman presents complaining of fatigue and heavy menstrual bleeds. Her Hb is 88 g/L (Low) and MCV is 67 (low).

The most appropriate management → **Oral Ferrous Sulphate**.

She has **Iron deficiency Anemia** 2ry to **menorrhagia**. We give **oral iron supplement**.

Blood Transfusion is indicated if:

♠ **Hb < 80 g/L** + **Symptoms of Anemia**. Or:

♠ **HB < 70 g/L** + With or Without **Symptoms of Anemia**.

Key 12

Henoch-Schönlein Purpura (HSP)

- Purpura is **non-blanching** and mainly on the **buttocks** and **Lower Limbs**.
- Precipitated by **URTI – Sore Throat**.
- All Blood Results are **NORMAL** "Normal Hb, WBCs and Platelets".

Others:

- **Arthralgia** "Esp. Knee".
- ↑ ESR, ↑ IgA.
- **Rarely, impaired renal function tests.**
- Rx → **Self-limiting** (e.g. Aspirin for arthralgia Unless there is renal impairment).

HSP → **PAAN**: **P**urpura, **A**rthralgia, **A**bdominal pain, **N**ephropathy "not always" (Hematuria, Proteinuria).

Example (1),

A 10 YO boy presents with a low-grade fever and macular rash especially on the back of the legs following an upper respiratory tract infection. A few hours later, these macules have turned into purpuric lesions that do not blanch on glass test. The boy also complains of joint stiffness and headache.

Hb (124 g/L) ▌WBC (3.3 X 10^9/L) ▌Platelets (219 X 10^9/L).

The Likely Dx → **Henoch-Schonlein Purpura**.

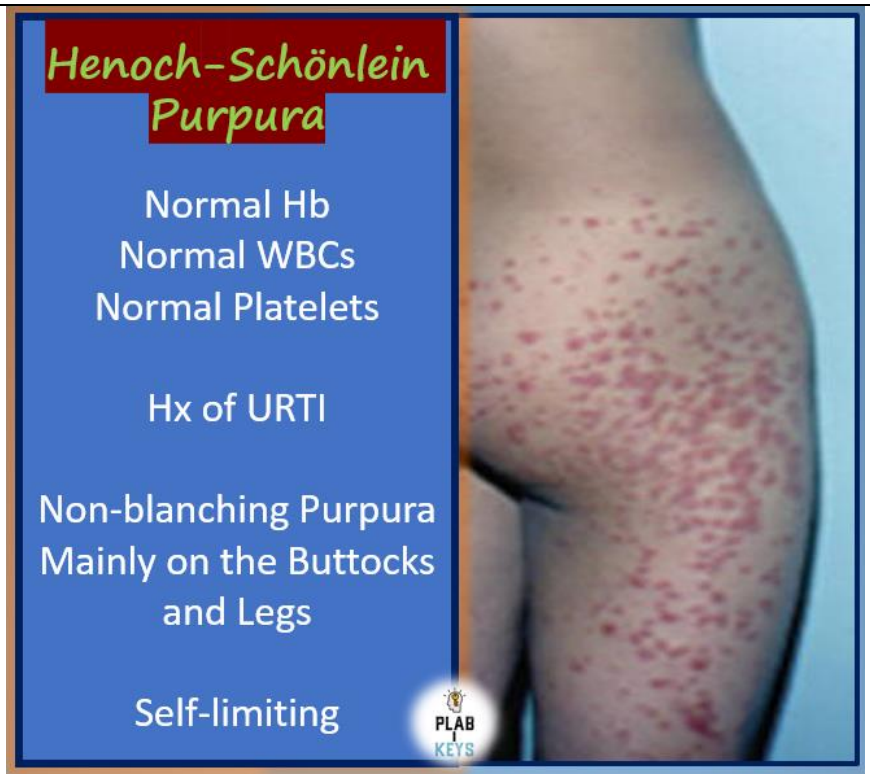
Note that Hb, WBCs, and platelets are normal.

Please note that if a patient presents with similar features but with LOW PLATELETS and normal Hb and WBCs, the answer would be → Idiopathic Thrombocytopenic Purpura (Explained Later in Key 17).

Example (2),

17 YO boy presents with palpable rash on his buttocks and extensor surfaces of his arms and legs that started following sore throat. He also has crampy abdominal pain, joint stiffness and joint pain. Urine Testing reveals microscopic hematuria and proteinuria.

The Likely Dx → **Henoch-Schonlein Purpura**.



Key 13

A 14 YO male presents with mucosal bleeding, petechial rashes, tiredness and pallor.

Hb 77 ▌WBCs 1.8 ▌Platelets 30 ▌Neutrophils 0.1

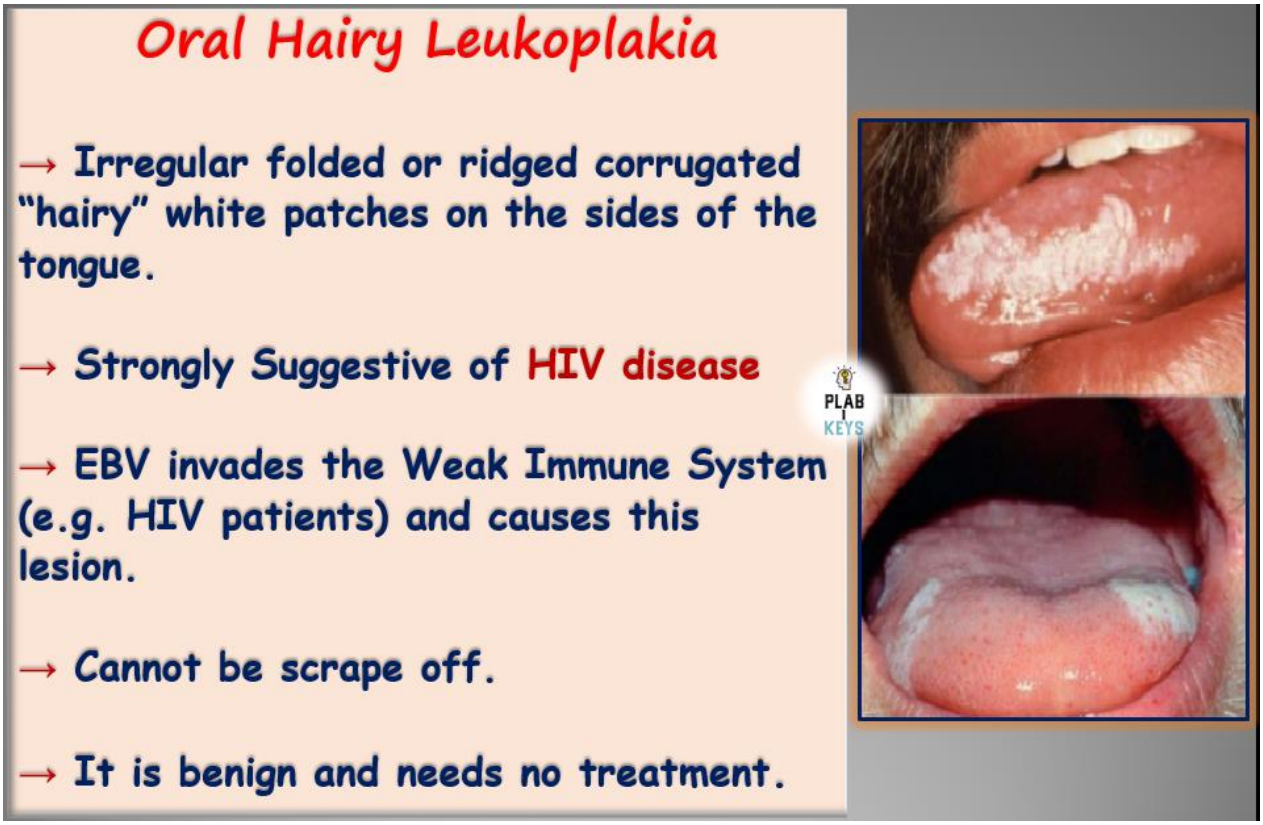
Blood Film shows Unremarkable "Normal" Morphology. Absent Reticulocytes. Bone Marrow Aspirate shows a marked reduction in all haemopoietic tissues replaced by fat spaces.

The likely Dx → **Aplastic Anemia**.

Pancytopenia = ↓ Hb, ↓ WBCs, ↓ Platelets

♦ In the exam, ***pancytopenia*** is either **Acute Lymphocytic Leukemia** or **Aplastic Anemia**. BM biopsy can differentiate.

	BM Aspirate/ Biopsy → **Numerous Blasts** → **Acute Lymphocytic Leukemia "ALL"** BM Aspirate/ Biopsy → **Reduction in all haemopoietic tissues replaced by fats spaces** → **Aplastic Anemia**. ♦ Unremarkable Morphology rule out Leukemia. ♦ In **Aplastic Anemia**, 2 of the following 3 must be present: **Hb < 10 ▌Platelets < 50 ▌Neutrophils < 1.5**
Key 14	**Hairy Leukoplakia** → **Irregular folded or ridged white patches on the sides of the tongue**. → Supportive of a Dx of **HIV disease** → **EBV** invades the Weak Immune System (e.g. HIV patients) and causes this lesion. → Cannot be scraped off. → It is **benign** and needs **no treatment**.

	A 42 YO ♂ presents with mild fever, tiredness, marked weight loss recently and bilateral white corrugated lesions on the lateral surfaces of his tongue. The likely Dx → **HIV Disease**. 
Key 15	◙ **The target INR in most cases "Including Warfarin intake for AF, DVT"** → **2-3** ◙ The target INR in **mechanical valve replacement "Metallic Valve"** → **3-4**

Key 16	50 YO ♂ complains of headache, pruritus, Hx of DVT. Hb: 190 g/L ▌WBCs: 15 X 10^9/L ▌Platelets: 802 X 10^9/L. The likely Dx → **PRV "Polycythemia Rubra Vera"** The Main Treatment line → **Venesection "Phlebotomy"** **In PRV:** √ Pruritus (Especially after hot shower) ▌Gout ▌Burning sensation of fingers and toes ▌Splenomegaly ▌Headache …etc √ All three cell lines are elevated (**High Hb**, **WBCs** and **Platelets**). √ Low/normal serum erythropoietin. √ **Hyperviscosity** ► High risk of **DVT**, **Pulmonary embolism**…etc.

Key 17

Idiopathic Thrombocytopenic Purpura (ITP)

- Mainly affects **children**, but can occur in adults.
- In children, it is usually proceeded by **infection**.
- **Isolated Thrombocytopenia** (Low Platelets but other labs are normal).
- **Bleeding**, **epistaxis**, **petechia**, **menorrhagia**. Sometimes Asymptomatic.
- **Rx** →

√ Prednisolone,

√ IV Ig (IV immunoglobulins).

√ Life-threatening hemorrhage (platelets < 20) → Emergency Platelet Transfusion.

If you see Isolated Thrombocytopenia ± Bleeding → Think of ITP.

Key 18

Normal PT: 10-14 sec.

Normal PTT: 35-45 sec.

Bleeding Time: 3-9 minutes.

- **↑ PTT** + (Bleeding into muscles or joints or easily bleeding)

→ think of **haemophilia**.

- **↑ PTT** and **↑ Bleeding Time** + (Mucosal Bleeding)

→ think of **VWD** "Von Willebrand Disease".

- **↑ PTT** and **↑ PT** and **↑ Bleeding Time** +

(Bleeding at any site e.g. purpura, petechia, GIT, ENT, venepuncture site)

→ think of **DIC**. (Others: ↓ Platelets and fibrinogen ▌↑ D-dimer)

Example,

14 YO ♂ has developed excessive bleeding after tooth extraction. He notes that he bruises easily with mild trauma.

Hb 120 g/L ▌WBC 7 ▌PT 12 ▌PTT 84 ▌Bleeding time: normal

◙ The likely Dx → **Haemophilia**.

◙ Haemophilia A or B → **Haemophilia A** (More common).

Isolated Prolonged PTT → Hemophilia. (see the notes above)

Key 19

Hemophilia A	Hemophilia B = "Christmas Disease"
More common (90% of the cases)	Less common
Factor **VIII** (8) deficiency.	Factor **IX** (9) deficiency.
Rx: √ **Desmopressin** (it increases Factor 8) √ Major bleeding → Recombinant factor VIII.	Rx: √ Desmopressin has **no role**. √ **Recombinant factor IX** (of choice).
Important: DO NOT give NSAIDs or IM injections in hemophilia (↑ bleeding)	

◙ Notes:

• **↑ PTT** + Normal PT and Bleeding Time

+ (Bleeding into muscles or joints or easily bleeding or after tooth extraction)

→ think of **haemophilia**.

• Haemophilia is **X-linked recessive** → mainly affects **Males**.

• Important X-linked recessive conditions → G6PD def., DMD, Hemophilia.

• Important: **Hemophilia B** is also called → **Christmas Disease**

Example,

6 YO boy, recurrent attacks of hemarthrosis (bleeding into knee and elbow joints). Factor VIII/XI assay shows low factor VIII.

The likely Dx → **Haemophilia A**.

The most appropriate treatment → **Desmopressin**.

Key 20

Scenario

40 YO ♀ presents with tiredness that started 2 weeks ago. She is mildly jaundiced. HR 78, BP 120/70. Labs are as follow:

Hb 92 g/L ▌MCV 98 fL (high, the normal range is : 76-96) ▌WBCs 8 ▌ Bilirubin 39 (high) ▌ALT, AST, ALP, Gamma Glutamyl Transferase: normal.

◙ The appropriate Investigation → **Direct Antiglobulin (Direct Coomb) Test**.

Here we have Anemia + High MCV + High Bilirubin → there is **hemolysis**!

Anemia + High Bilirubin = Hemolysis

What about the High MCV?

We know that macrocytic anemia (Folate and Vit. B12 Deficiency) shows high MCV; however, hemolytic anemia can sometimes show high MCV.

Markers of Hemolysis:

↑ LDH, ↑ Indirect Bilirubin "Jaundice", ↑ Reticulocytosis, Sometimes ↑ MCV and MCHC indicate hemolysis.

Direct Antiglobulin (= Direct Coomb) Test

→ Autoimmune Haemolytic Anemia.

Indirect Antiglobulin (= Indirect Coomb) Test

→ Cross-Matching (blood transfusion preparations) / Antenatal Screening.

Key 21

Scenario

38 YO ♀ presents with tiredness. She is mildly jaundiced. Hx of URTI.

Labs are as follow:

Hb 92 g/L | MCV 99 fL (normal: 76-96) | WBCs (4-11) | Bilirubin 29 (high)

ALT, AST, ALP and Gamma Glutamyl Transferase are normal.

Peripheral Blood Smear show → **Polychromasia** + **Spherocytes**.

- This is most likely is a case of Autoimmune hemolytic anemia.
- **Markers of Hemolysis:**

↑ LDH, ↑ Indirect Bilirubin "Jaundice", ↑ Reticulocytosis,
Sometimes ↑ MCV and ↑MCHC indicate hemolysis as well.

Request → Direct Coomb Test | Also known as Direct Antiglobulin test.

◙ **In this scenario:**

Anemia + ↑ bilirubin (jaundice) + ↑ LDH + ↑ MCV and MCHC

→ Anemia with Hemolysis

→ Direct coomb (antiglobulin) test to confirm autoimmune hemolytic anemia.

• **Polychromasia** = ↑↑↑ immature RBCs.

• **Spherocytes** → Hereditary Spherocytosis**?** Nope! Not necessarily! Spherocytes can be seen in both Hereditary Spherocytosis and Autoimmune Hemolytic Anemia. To Differentiate → **Direct Coomb Test**.

In this scenario, although we suspect hereditary spherocytosis, Direct Coomb "**Direct antiglobulin**" test would differentiate the cause of the hemolysis. This is because it will be **+ve** in Autoimmune Hemolytic Anemia, and **-ve** in Hereditary Spherocytosis.

Osmotic Fragility Test is **positive** in both **Hereditary Spherocytosis** and **Autoimmune hemolytic anemia**.

Direct coomb "antiglobulin" test is **positive** in Autoimmune hemolytic anemia and **negative** in Hereditary Spherocytosis.

Thus, Direct coomb is more appropriate as it can differentiate the 2 cases.

Autoimmune hemolytic anemia:

√ Spherocytes.

√ +ve Osmotic Fragility test.

√ +ve Direct Coomb test.

Hereditary Spherocytosis:

√ Spherocytes.

√ +ve Osmotic Fragility test.

√ -ve Direct Coomb test.

Key 22	An elderly man with dementia, recurrent visits to the hospital for **bruises** in the **face**, **head** and **forearms**. → Suspect "**non-accidental injury**". Someone is abusing this old man as the bruises are in suspicious sites. If the cause was "recurrent falls" for instance, the bruises would have been over the hip, knee or shoulder joints, not in the face! And not on several distant body areas!
Key 23	• **HELLP Syndrome** → **H**emolysis (low Hb), **E**levated **L**iver enzymes, **L**ow **P**latelets. • **Acute Fatty Liver of Pregnancy (AFLP)** → **ELLP** (without **H**emolysis) + (↓) Glucose ± (↑) Ammonia • **Disseminated Intravascular Coagulation (DIC)** → High PT, High PTT, High Bleeding Time, Low Platelets, Low Fibrinogen

Example,

A pregnant woman in her 35 weeks pregnancy developed sudden severe (acute) abdominal pain and is taken for emergency C-Section. Her BP 110/60. Labs:

Hb: 101 ▌WBC 9.5 (Normal) ▌Platelets 65 (Low) ▌PT 28 sec (high) ▌PTT 67 sec (high) ▌Fibrinogen 0.7 (low) ▌Bilirubin 23 (high)

The likely Dx → **Disseminated Intravascular Coagulation (DIC)**.

High PT, PTT

Low Platelets, Fibrinogen

→ **DIC** (see the comparison above)

◙ Remember: **DIC Triggers**→ sepsis, surgery, major trauma, cancer, and **complications of pregnancy**

This lady might have developed Placenta abruption which has led to DIC.

Key 24

Scenario (1)

A 4 YO boy has easy bleeding into joints following a minor trauma. His uncle and grandfather had the same condition.

The likely mode of inheritance → **X-linked**.

◙ 2 ways to answer this question:

1 √ This is likely a case of **hemophilia** which is **X-linked recessive**. (Bleeding into joints and muscles is common in Haemophilia -factor type bleeding-).

2 √ The fact that all the affected individuals mentioned in the stem are **males** (the little ***boy***, the ***uncle*** and the ***grandfather***) makes it more likely to be **X-linked**.

Scenario (2)

A 16 YO girl presents with profuse bleeding after a dental extraction. Her father and paternal grandmother have experienced similar problems.

The likely mode of inheritance → **Autosomal Dominant**.

√ This likely a case of **VWD** "**Von-Willebrand Disease** → Mucosal Bleeding + NOT X-linked".

√ Most Cases of **VWD** are → **Autosomal Dominant**.

√ This scenario **CANNOT be X-linked** as a **girl** and a **grandmother** (**females**) are affected. In X-linked diseases, nearly only males are affected or at least

can show symptoms (The other X in Females can compensate for the affected X).

In this scenario, the paternal grandmother has passed the condition to the father (male), and the father has passed it to his daughter (girl).

A father with an X-linked condition has ZERO chance to inherit the condition to his **Sons**. However, 100% of his **daughters** will be carriers.

◙ A Quick Recap:

√ **Hemophilia** → X-linked Recessive.

√ **G6PD deficiency** → X-linked Recessive.

√ **VWD** → Mostly Autosomal Dominant.

√ **Hereditary Spherocytosis** → Mostly Autosomal Dominant.

√ **Thalassemia** → Autosomal Recessive.

√ **Sickle Cell Anemia** → Autosomal Recessive.

◙ Autosomal **Recessive** Conditions: (25% if **both parents** are **carriers**)

◙ Autosomal **Dominant** Conditions: (50% if **One parent** is **affected**)

◙ X-linked **Recessive** Conditions: (**Male**: 50% if **mother** is **carrier**)

Key 25

◙ Cytochrome P450 Enzyme **Inducers** → ↓ the anticoagulant effect of the Warfarin → ↓ INR.

◙ Cytochrome P450 Enzyme **Inhibitors** → ↑ the anticoagulant effect of the Warfarin → ↑ INR.

Inducers → Decrease

Inhibitors → Increase

Examples:

P450 Enzyme Inducers (CRAP GPs)	P450 Enzyme Inhibitors (SICK-FACES.COM)
Decreases Warfarin effect → ↓INR	**Increases** Warfarin effect → ↑ INR
If used with COCP, additional contraceptive method is needed (e.g. Depo-Provera, IUS, barrier methods) as these enzyme inducers **weaken** the COCP and POP.	If used with COCP, no need to change anything.

• **C**arbamazepine • **R**ifampin • **A**lcohol "Chronic" • **P**henytoin • **G**riseofulvin • **P**henobarbital • **S**ulphonylureas	• **S**odium Valproate. • **I**soniazid. • **C**imetidine. • **K**etoconazole. • **F**luconazole. • **A**lcohol (Acute drinking). • **C**hloramphenicol. • **E**rythromycin (Macrolides: **Clarithromycin**) • **S**ulfonamides. • **C**iprofloxacin. • **O**meprazole. • **M**etronidazole

Example,

An elderly ♀ presents with chest infection and thus was started on clarithromycin. Her Hx includes, taking Carbamazepine for trigeminal neuralgia, taking Warfarin for mechanical valve replacement, taking Bisoprolol, Amlodipine and Atorvastatin. Her INR was found to be 1.4 (The target for mechanical valve replacement is 3-4). What is the causative drug for this low INR?

The answer → **Carbamazepine**

◙ **Carbamazepine** is a P450 enzyme **inducer**; thus, it will **decrease** the anticoagulant effect of Warfarin and therefore leads to ↓ INR.

◙ **Clarithromycin** is a Macrolide (like erythromycin). It is a P450 enzyme **inhibitor** and thus leads to **increase** the anticoagulant effect of Warfarin and therefore ↑ INR.

◙ The remaining drugs in the stem has no effect on P450 enzyme.

Key 26

Management of High INR in Patients on Warfarin

◙ If MAJOR Bleeding:

√ Stop Warfarin.

√ Administer **IV Vitamin K1** (Phytomenadione).

√ Administer **Prothrombin Complex Concentrate** (If not available → FFP).

Note,

*Go for **Prothrombin Complex Concentrate (PCC)** first, not Fresh Frozen Plasma (FFP). If PCC is unavailable → FFP.*

*• If you are to pick between (PCC) and (Vit. K) in the exam, pick → **PCC**. This is because PCC works faster. In reality, we would give both in major bleeding.*

◙ If INR is > 8 ± Minor Bleeding:

√ Stop Warfarin.

√ Administer IV or oral **Vitamin K1** (Phytomenadione).

√ Restart warfarin when INR < 5.

◙ If INR 5-8 + Minor Bleeding:

√ **Stop Warfarin** and Check INR the following day.

√ Administer IV or oral **Vitamin K1** (Phytomenadione).

√ Restart warfarin when INR < 5.

(Similar to the above one).

◙ If INR 5-8 + NO Bleeding:

√ **Stop Warfarin and Check INR the following day**.

√ Administer IV or oral **Vitamin K1** (Phytomenadione).

√ Restart warfarin when INR < 5.

(Similar to the above one but here no bleeding and so no vitamin K).

So, if the INR between 5 and 8, stop warfarin and restart it when INR is < 5. (This is in all cases). If WITH minor bleeding (eg, epistaxis), give vitamin K. If No bleeding, no need for vitamin K.

◙ If INR < 5 (But still higher than the target level):

√ Reduce "Or" Omit one or two doses of Warfarin.

√ Measure INR in 2-3 days.

Note that:

♦ **Major Bleeding** → **Intracranial Bleeding, GIT Bleeding, Internal large vessels bleeding (eg, leaking abdominal aortic aneurysm).**

♦ **Minor Bleeding** → **Epistaxis, Hematuria**.

Example **(1),**

After a fall, an elderly patient on Warfarin and atenolol for Atrial Fibrillation was brought to the ER. CT head shows 1X2 cm Cerebral Hematoma. INR is 3.4. The patient is given IV 5 mg Vitamin K1. What should be given Next?

→ **Prothrombin Complex Concentrate**.

This is a case of **Major bleeding** (Intracranial Bleeding). We should:

1) ***Stop Warfarin***.

2) Give IV 5 mg ***Vit. K1***.

3) Give ***Prothrombin Complex Concentrate***.

Note: The target INR in patients on Warfarin for AF → 2-3 (Here, it is a bit higher)

Example (2),

An elderly patient with a Hx of Atrial Fibrillation on Warfarin was found to have INR of 6.7. He is on Warfarin. What should be done at the anticoagulant clinic?

→ **Stop Warfarin, Repeat INR the Next day**.

(**INR 5-8 with or without minor bleeding**) → STOP WARFARIN and Restart when INR is < 5.

Example (3),

An elderly patient with a Hx of Atrial Fibrillation on Warfarin presents with non-stop epistaxis. His INR is 8.1. What should be done?

→ **Give Vitamin K**.

Note that Epistaxis is a minor bleeding.

◙ If INR is > 8 ± Minor Bleeding:

√ Stop Warfarin.

√ Administer IV or oral **Vitamin K1** (Phytomenadione).

Example (4),

◙ A man on warfarin fell and presents with confusion. His INR was found to be 6. What should be done?

We suspect he has an intra-cranial hemorrhage (namely: **subdural hematoma**)

Elderly + on warfarin + Hx of fall + presents with confusion/ headache

Suspect → **Subdural hematoma** (In Neurology chapter).

Since **intracranial hemorrhage** is a **Major Bleeding**,

we give → **Prothrombin complex concentrate**.

Remember:

◙ If MAJOR Bleeding:

√ Stop Warfarin.

√ Administer IV Vitamin K1 (Phytomenadione).

√ Administer Prothrombin Complex Concentrate (If not available → FFP).

*Note, Go for **Prothrombin Complex Concentrate** first, not Fresh Frozen Plasma.*

Example (5),

◙ A man presents to the ER with epistaxis for the last 4 hours. Despite nasal packing and cautery, the nosebleed continues. His blood pressure is 77/41 mmHg. He takes warfarin for atrial fibrillation. His INR is 7 (target is 2-3). What is the most appropriate **INITIAL** step in managing this patient?

→ **IV fluids**.

• Note that the patient is **haemodynamically unstable** (his SBP is < 90 mmHg) and the question asks about the **INITIAL** step! We need to stabilise him first with IV fluids or even blood transfusion in required.
• Be careful to the word (**initial** management)!

Example (6),

◙ A 63-year-old man with history of abdominal aortic aneurysm presents with sudden onset severe abdominal pain. He is on warfarin as he has a mechanical aortic valve replacement 6 years ago. Doctors suspect leaking abdominal aortic aneurysm. His blood pressure is 95/63 mmHg and HR is 120 bpm. What is the single most appropriate management?

A) Blood transfusion.
B) Prothrombin complex concentrate (PCC).
C) Vitamin K.
D) Fresh frozen plasma (FFP).
E) Protamine sulfate.

Answer → B.

• Internal large vessels bleeding (as in leaking AAA abdominal aortic aneurysm) is a major bleeding. This patient would need to stop warfarin → IV vitamin K → PCC (or FFP if unavailable).

• In this stem, both PCC and vitamin K are given.

*• If you are to pick between (PCC) and (Vit. K) in the exam, pick → **PCC**. This is because PCC works faster. In reality, we would give both in major bleeding.*

Example **(7),**

◙ A 47-year-old man with a history of mechanical aortic valve replacement and he is on warfarin for 7 years. He presents with non-stop epistaxis despite nasal packing and cautery. His INR is 7. His blood pressure is 110/75 mmHg. His hemoglobin is 111 g/L (130-180). What is the most appropriate management?

A) IV fluid.

B) Vitamin K.

C) Prothrombin complex concentrate (PCC).

D) Blood transfusion.

E) Tranexamic acid.

Answer → B.

◙ He has **INR between 5 and 8 + Minor Bleeding** (Epistaxis):

√ Stop warfarin.

√ Administer IV vitamin K.

√ Restart warfarin when INR is < 5.

◙ So, the valid answer here is to → **Give Vitamin K**.

◙ If **INR is 5-8 but with NO bleeding** → The same but without IV vitamin K.

◙ **Let's check the other options:**

- **PCC**: is given if there is Major bleeding (eg, intracranial, GIT, aneurysmal).
- **IV fluids**: it is good to be given as initial to prevent hypovolemia. However, the patient's BP here is normal, the question asks about the most appropriate not the initial Rx, and more importantly, vitamin K would stop bleeding whereas IV fluids would not.
- **Blood transfusion**: is not required unless Hb is < 70 g/L (however, it is a good practice here to request a group and save, a cross-match blood).

	• **Tranexamic acid**: Can be helpful but the guidelines recommend vitamin K in this situation.
Key 27	Anemia (**Low Hb**) + High **(↑) MCV** "Mean Cell Volume" → **Macrocytic Anemia** → (**Folate deficiency** anemia Or **Vit. B12 Deficiency** anemia). **In Vitamin B12 Deficiency** → √ **Oval Macrocytic RBCs**. (↑ MCV). √ **Hypersegmented Neutrophils**. ◙ **Some clues towards Vit. B12 Deficiency:** • The patient is **Vegan** (as Vit. B12 exists in Fish, meat, Dairy products). • **Peripheral Paraesthesia "Pins and Needles sensation"**, Loss of position and Vibration sense, Ataxia, confusion. • Common Features of **Anemia** → Fatigue, Pallor, Dyspnea on effort. ◙ **Important Note:**

Even though "**Angular Stomatitis**" is a known sign of "**Iron Deficiency Anemia**", ***it still can occur in Macrocytic Anemia "Folate/ Vit. B12 Deficiency".***

◙ **Rx →** **Hydroxocobalamin**

Key 28

DVT "Deep Vein Thrombosis"

◙ Some Risk Factors:

Smoking ▌**Immobility** ▌**Long sitting** "e.g. **long trip**" ▌**Major surgery**

◙ Some Signs

√ Calf swelling, **Tenderness**, **warmth** and **redness**.

√ Passive movement causes pain.

√ One calf has a larger diameter than the other.

Example,

62 YO smoker ♂ has undergone hip replacement surgery 3 days ago. His left leg is swollen and tender. The diameter of left calf is larger than the right calf. The calf is tender on touch.

→ **Deep Vein Thrombosis (DV)**.

	RFx here → ***Smoking***, ***Immobility***, ***Major Surgery***.
Key 29	**Secondary Polycythemia** ♦ Remember in **Polycythemia Rubra Vera "PRV" (Primary Polycythemia), all 3 cell lines Hemoglobin, WBCs and Platelets are Elevated**. ♦ In **Secondary Polycythemia**, **Only Hemoglobin is Elevated**. ♠ One **important cause** of 2ry Polycythemia to remember is **Chronic Hypoxia** (such as those who are **chronic smokers → COPD**). Other causes → High Altitudes/ Cyanotic Congenital Heart diseases. ♠ Chronic Hypoxia → Stimulates the kidneys to produce more and more **Erythropoietin** → Which stimulates the bone Marrow to produce → More and more RBCs so they can carry more O2 to the tissues. ***Important note*** √ In **Primary** Polycythemia → **Erythropoietin** is either **Low** or **Normal**. √ In **Secondary** Polycythemia → **Erythropoietin** is **High**. ***Example,***

A 55 YO ♂ presents with shortness of breath and chronic cough. He is chronic smoker and drinks alcohol socially. He also complains of tiredness and lethargy.

His Hb is 195 g/L ▌WBCs 9 ▌Platelets 270 ▌Hematocrit 58%

The useful hormone level to request is → **erythropoietin**.

◘ **Erythropoietin would be high in 2ry Polycythemia.**

◘ **Note that only Hb and Hematocrit are high. WBC and Platelets are normal.**

◘ **He is a chronic smoker with chronic cough (COPD) "one important cause of hypoxemia and therefore 2ry Polycythemia".**

Remember,

√ In **1ry Polycythemia** "Polycythemia Rubra Vera"

→ Request **JAK Mutation Screen**.

√ In **2ry Polycythemia**

→ Request **Erythropoietin**.

Key 30	Hemolytic Uremic Syndrome (HUS)	Thrombotic Thrombocytopenic Purpura (TTP)

Triad: **1) Hemolytic Anemia** **2) Uremia (Acute Renal Failure)** **3) Thrombocytopenia (Low Platelets)** ♦ ***Children***	**Pentad**: **1) Hemolytic Anemia** **2) Uremia (Acute Renal Failure)** **3) Thrombocytopenia (Low Platelets)** **4) Neurological Manifestations** **5) Fever**
Eating Undercooked Contaminated food → **E. Coli** O157 → Produce Verotoxin → Profuse Diarrhea → Bloody Diarrhea → (after 2-14 days) → Uremia "Acute Renal Failure" (Hematuria, Proteinuria, ↑ Urea and Creatinine) So, remember: • **Diarrhea** → turns **Bloody** → **Renal Failure** **(Acute Kidney Injury)** (Hematuria, proteinuria…etc).	ADAMTS 13 factor Deficiency or inhibition

± Features of Anemia (e.g. Pallor, Fatigue).	
Rx → **Supportive** √ **IV fluids**. √ ± **Blood Transfusion** √ ± **Dialysis** (if required) √ If Very Severe → Plasma Exchange ◙ **Never Give Antibiotics in HUS**! (More toxins are released as the E. Coli dies)	

Example (1),

9 YO girl presents with Pallor, Hematuria, Proteinuria, ↑ Urea and Creatinine. 4 Days ago, this girl had Bloody Diarrhea.

The Likely Diagnosis → **Hemolytic Uremic Syndrome (HUS)**

Example (2),

A 5-year-old girl with 5 days history of bloody diarrhoea and dehydration. Blood culture shows E. coli. Lab shows that: Serum Na^+ is low, serum K^+ is high, serum Urea and Creatinine are high, Serum Calcium is Normal, Serum Bicarbonate is low. What is the like diagnosis?

a. **Acute kidney injury**

b. Addison's

c. Renal tubular acidosis

√ This is a classic case of HUS (Hemolytic-Uremic Syndrome).

√ **HUS** is the most common cause of **acute kidney injury** in **children** and is increasingly recognized in adults.

Example **(3),**

A 44-year-old woman presents to the ER with a diagnosis of hemolytic uremic syndrome. Over the last week, she has been experiencing fatigue, dizziness, and shortness of breath. Lab and examinations reveal pallor, tachycardia, hypotension, low serum hemoglobin (60 g/L), moderately deteriorated renal function tests. What is the most appropriate initial management?

→ Immediate administration of packed red blood cells transfusion.

	• **Remember**: the management of HUS "hemolytic uremic syndrome" is supportive (eg, blood transfusion, dialysis, IV fluids). • This patients' symptoms (fatigue, dizziness, tachycardia, pallor, shortness of breath) are caused by the **severe anemia**. Thus, **RBCs transfusion** is more appropriate than dialysis initially in this case. • Remember: in HUS, do not give antibiotics.
Key 31	***Scenario*** 66 YO ♂ presents with Hoarseness of voice. He has a Hx of weight loss recently. Chest X ray shows opacity in the right upper mediastinum. There is no Shortness of breath. What is the single best Investigation to diagnose? Answer → **Lymph Node Biopsy** This is a tricky question. ◙ Opacity/ mass in the **superior mediastinum** could be one of the (**5 Ts**) √ **T**errible Lymphoma. √ **T**hymus (Thymoma). √ **T**horacic Aortic Aneurysm √ **T**hyroid Goitre/ Neoplasm. √ **T**eratoma. ◙ Looking at the History**, No SOB** or **Cough** → **R/O Lung carcinoma**.

	◙ There is a Hx of **Weight Loss** + **Old Age** → The best one of the 5 Ts that fits well here is **Lymphoma**. ◙ **To Diagnose Lymphoma, Lymph Node Biopsy is required.** ◙ Note, Lymphoma can compress a Unilateral Recurrent Laryngeal Nerve leading to Hoarseness of voice. ◙ **Additional Notes to help you correlate topics:** • Left Supraclavicular Mass → Virchow's Node → Indicative of **Gastric Carcinoma** (Anorexia, Dyspepsia, Weight Loss, Old age). This sign is called → **Troisier's sign**. • Right Supraclavicular Mass → **Oesophageal cancer**, **Lung cancer**, **Hodgkin's Lymphoma**. • **Pancoast Tumour** → A tumour of the **Apex of the Lung** (located at the top end of either the left or the right lung). It typically spreads to the nearby tissues such as the ***Ribs*** and the ***Vertebrae***. Most Pancoast tumours are Non-small cell lung cancer.
Key 32	**Blood Transfusion is indicated if:** ♠ **Hb < 80 g/L** + **Symptoms of Anemia**. Or: ♠ **HB < 70 g/L** + With or Without **Symptoms of Anemia**.
Key 33	**Macrocytic Anemia** (High MCV) + Associated **Autoimmune Disease** (e.g. Vitiligo, Hypothyroidism, DM type 1, Psoriasis etc)

→ Think of **Pernicious Anemia**.

Pernicious Anemia → **Autoimmune** gastric atrophy → Loss of gastric **intrinsic factors** → impaired Vit. B12 absorption → **Vit. B12 deficiency**.

◙ Management in such a case would be

→ **Intramuscular Hydroxocobalamin -Vit B12-** (not Oral, nor IV). *Important √*

Example (1),

44 YO ♀ presents with tiredness and fatigue. Her Hb is 88 g/L (Low), **MCV** is 125 (**High**). **Vitiligo** is noted on her hands.

The likely Dx → **Pernicious Anemia**. Another Valid → **Vit. B12 deficiency**.

√ Pernicious Anemia is an **Autoimmune disease**. It causes Vit. B 12 deficiency (High MCV = Macrocytic Anemia). Presence of another Autoimmune disease (such as Vitiligo, Hypothyroidism) supports the Dx of Pernicious Anemia.

√ Given the elevated MCV and her autoimmune history (eg, vitiligo, hypothyroidism, DM-1), **vitamin B12 deficiency** is the most likely cause of her anaemia, likely due to **pernicious anaemia**. This condition is common in individuals with other autoimmune diseases, where the body's immune system attacks cells in the stomach, reducing intrinsic factor production, which is essential for vitamin B12 absorption. The reduced B12 levels impair red blood cell production, leading to macrocytic anaemia.

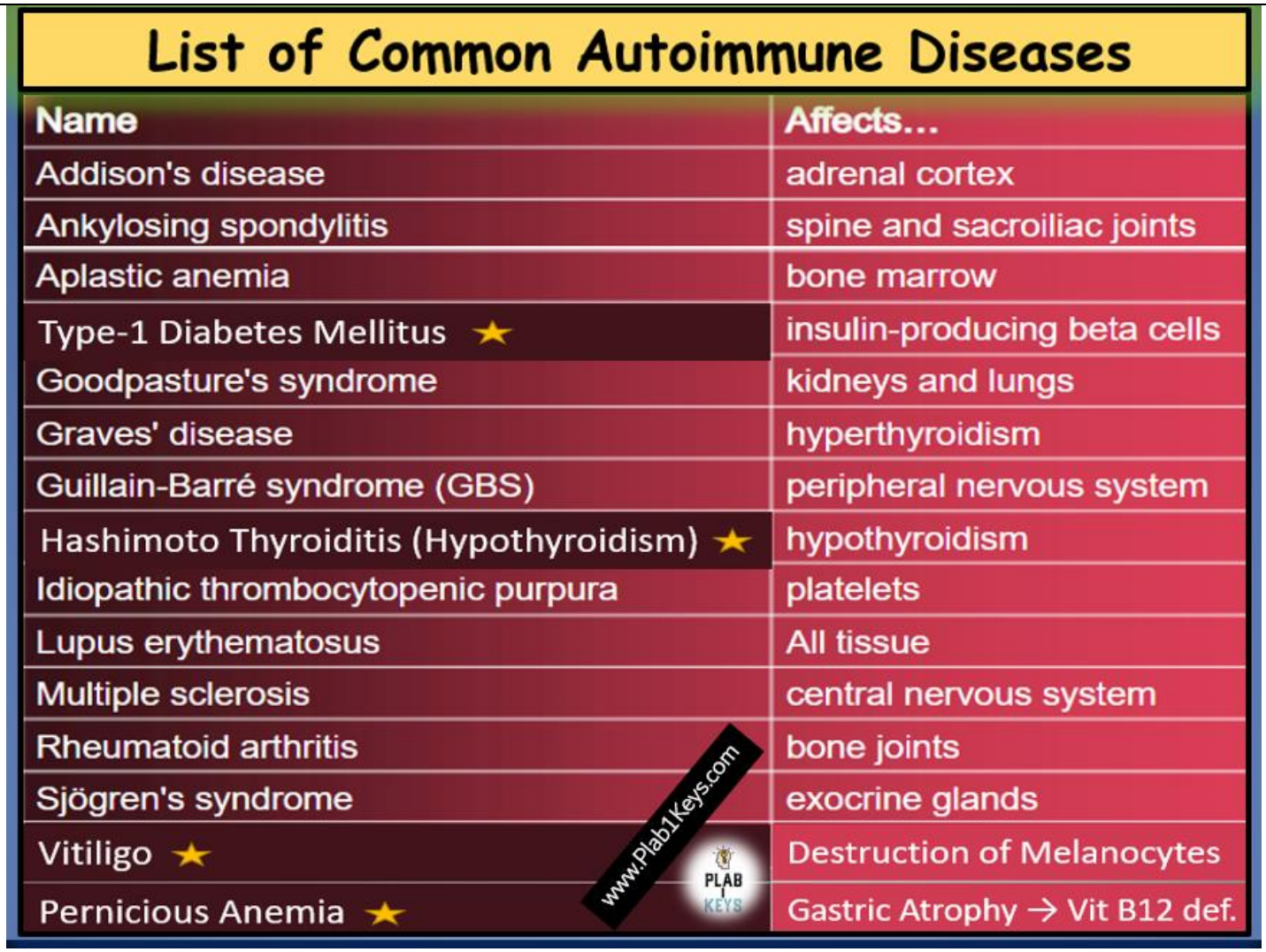
√ While **folate deficiency** can also cause macrocytic anaemia, in patients with autoimmune backgrounds, B12 deficiency is more likely. In clinical practice, B12 levels would be measured to confirm the diagnosis.

Example (2),

A 44 YO ♀ presents with tiredness and fatigue. Her Hb is 88 g/L (Low), **MCV** is 125 (**High**). She also complains of constipation, coarse dry skin, hair loss and cold peripheries.

The likely Dx → **Pernicious Anemia**.

	She has Hypothyroidism (which is mostly an Autoimmune disease - Hashimoto thyroiditis). **Macrocytic Anemia** + Associated **Autoimmune disease (such as Vitiligo/ Hypothyroidism)** → **Pernicious Anemia**. Another → **Vitamin B12 deficiency**. **List of Common Autoimmune Diseases**



List of Common Autoimmune Diseases

Name	Affects...
Addison's disease	adrenal cortex
Ankylosing spondylitis	spine and sacroiliac joints
Aplastic anemia	bone marrow
Type-1 Diabetes Mellitus ★	insulin-producing beta cells
Goodpasture's syndrome	kidneys and lungs
Graves' disease	hyperthyroidism
Guillain-Barré syndrome (GBS)	peripheral nervous system
Hashimoto Thyroiditis (Hypothyroidism) ★	hypothyroidism
Idiopathic thrombocytopenic purpura	platelets
Lupus erythematosus	All tissue
Multiple sclerosis	central nervous system
Rheumatoid arthritis	bone joints
Sjögren's syndrome	exocrine glands
Vitiligo ★	Destruction of Melanocytes
Pernicious Anemia ★	Gastric Atrophy → Vit B12 def.

Key 34

In a patient with Megaloblastic Anemia where **both Vitamin B12 and Folic Acid are deficient:**

→ Start with **IM Vitamin B12** (Hydroxocobalamin)

and **then** give **Oral Folic Acid** when Vitamin B12 level is normal.

	Mnemonic: The letter **B** is before **F** So, treat vitamin **B**12 deficiency before **F**olic acid deficiency.
Key 35	**Tumor Lysis Syndrome** → **UK Pc** Hyper**U**ricemia (↑ **Uric Acid** "Also called **serum Urate**) → Gout. Hyper**K**alemia (↑ K^+ "**Potassium**") Hyper**P**hosphatemia (↑ **Phosphate**) Hypo**c**alcemia. (↓ **Calcium**). The most specific one of the above → **↑ Urate** (uric acid) serum levels. √ It occurs mainly in Leukemia (Especially **ALL**) and Lymphoma (Particularly **Burkitt's Lymphoma**) after initiating **Chemotherapy**. √ Chemotherapy, Radiotherapy, Surgery → **Rapid Lysis of Tumour Cells** → Excessive amounts of Uric acid "Urate", Potassium and Phosphate are released into the blood. √ Ok, Why Calcium is low then? This is because phosphate is high :D. Just memorise that Phosphate and Calcium counter each other.

◙ It is a **hemato-oncological emergency** as it rapidly leads to **Renal Failure** (***High Urea and Creatinine***), Cardiac and Neurological Complications.

◙ Management is complicated; however, **remember that IV fluid is an important part of the management.**

Example,

35 YO ♂ with Burkitt's Lymphoma has started chemotherapy 2 weeks ago and now is presenting with feeling lethargic and passing very little amounts of urine.

Potassium is High ▌Urea and Creatinine are High ▌serum Calcium is low.

The likely Dx → TLS (**Tumour Lysis Syndrome**)

The single best Investigation that would help in management

→ **Serum Urate**.

Attention, please, some students get confused with the word (Urate). It is the same as (Uric Acid)!

	Explaining the Question: In this stem, it gives you the Hx of Burkitt's lymphoma + Chemotherapy. And then the stem shows that the patient has developed Renal Failure (high urea and creatinine). Finally, it gives you 2 out of the 4 pathognomonic labs for Tumour lysis syndrome (**High Potassium** and **Low Calcium**). Low calcium would mean "**High Phosphate**". The remaining one is the **Serum Urate** "Uric Acid".
Key 36	**Pregnancy Trimesters by Weeks** 

TRIMESTER	MONTH	WEEK
1	ONE	1-4
	TWO	5-8
	THREE	9-13
2	FOUR	14-17
	FIVE	18-21
	SIX	22-26
3	SEVEN	27-30
	EIGHT	31-35
	NINE	36-40

Anemia With Pregnancy

◙ When can we consider it Anemia?

√ In 1st trimester → if the Hb **< 11** g/dL.

√ In 2nd Trimester → If Hb **< 10.5** g/dL.

√ In 3rd Trimester → If Hb **< 10.5** g/dL.

√ **Post-Partum** → If Hb **< 10** g/dL.

Example,

A 28 YO Pregnant ♀ in her 28-week gestation presents for a regular antenatal visit. Her Hb is 11 g/dL.

→ **Normal Physiological Phenomenon** (**Not Anemia**)

→ **Reassure**

She is in the 3rd trimester. Anemia is considered if Hb < 10.5 in 3rd trimester.

	A Quick Note Some students might get confused with the **Hemoglobin Units**. Simply, 13 g/**dL**. Is the same as 130 g/**L**.
Key 37	Although **Anemia of chronic disease** is usually Normochromic Normocytic, it **can be** hypochromic microcytic such as in the cases of Rheumatoid Arthritis and Crohn's disease.
Key 38	**Hereditary Spherocytosis (In Points)** √ **FHx** "75% is **Autosomal Dominant**". √ High (↑) **MCHC** "Mean Cell Hemoglobin Concentration". √ Hemolytic Anemia (Jaundice, Reticulocytosis, High bilirubin), Gallstones. √ Blood film → **Spherocytes** and reticulocytes (**Spherocytes** are also present in Autoimmune Hemolytic Anemia -**AHA**-). √ **+ve Osmotic Fragility Test**. √ **-ve Direct Coomb "Antiglobulin" Test**. (***Direct Coomb "Direct Antiglobulin" Test is Used To differentiate between AHA and Hereditary Spherocytosis as it is +ve in AHA and -ve in H. Spherocytosis***). √ An Important Complication to remember → **Aplastic Crisis** "Due to **Parvovirus B19** infection".

√ **Important**: **Parvovirus B19 can cause aplastic anemia is Hereditary Spherocytosis and also in Sickle Cell Anemia (SCA).**

- **Parvovirus B19 (Aplastic Crisis)** → Severely **Low Hb** and **Low Reticulocytes**.
- **Splenic Sequestration Crisis** → Severely **Low Hb**, But **High Reticulocytes**.

√ Management Lines of H. Spherocytosis include Steroids, Folic Acid and Splenectomy.

Autoimmune hemolytic anemia:	**Hereditary Spherocytosis:**
√ Spherocytes.	√ Spherocytes.
√ +ve Osmotic Fragility test.	√ +ve Osmotic Fragility test.
√ +ve Direct Coomb test.	√ -ve Direct Coomb test.

Example (1),

A 20 YO ♂ presents with recurrent episodes of right upper quadrant pain. U/S reveals Gallstones. His father had splenectomy when he was young.

Hb is low ▌MCHC is high ▌WBCs and Platelets are normal.

The likely Dx → **Hereditary Spherocytosis**.

Points in favour:

√ Family Hx of splenectomy (Autosomal Dominant).

√ High MCHC.

√ Hemolysis → Gallstones.

"Chronic hemolysis leads to increased bilirubin excretion and pigment gallstones formation"

Example **(2),**

38 YO ♀ presents with tiredness. She is mildly jaundiced. Hx of URTI.

Labs are as follow:

Hb 92 g/L ▌MCV 98 fL (normal: 76-96) ▌WBCs 8 ▌Bilirubin 29 (high)

ALT, AST, ALP and Gamma Glutamyl Transferase are normal.

Peripheral Blood Smear → **Polychromasia** + **Spherocytes**.

◙ The appropriate Investigation → **Direct Antiglobulin (Direct Coomb) Test**.

Anemia + jaundice + high bilirubin → hemolysis.

• **Polychromasia** → ↑↑↑ immature RBCs.

• **Spherocytes** → Is it Hereditary Spherocytosis**?** Not necessarily! Spherocytes can be seen in both Hereditary Spherocytosis and Autoimmune Hemolytic Anemia. To Differentiate → **Direct Coomb Test**.

Key 39	Remember, in a patient presents with **Pancytopenia**, perform **BM Biopsy**: √ Numerous Blasts → **Acute Lymphocytic Leukemia** √ Hypoplastic bone marrow. (Reduction in hemopoietic cells) (Replaced by Fat) → **Aplastic Anemia**
Key 40	**If a blood donor went into (Coma) while donating blood, all the following could be effective:** **√** Ensure he is hydrated and has not skipped a meal. **√** Elevate his legs (as it might be due to a vasovagal attack). **√** Ensure his Hb meets the minimum requirements for donation. **√** Encourage him to eat, rest and mobilise after recovery. ***ATTENTION***, WE SHOULD NEVER Continue taking blood from him in this case! We need to **IMMEDIATELY** stop the donation.
Key 41	**Important**: ◙ Patients who are on **Warfarin** and are going for **Surgery** need to → **Stop their Warfarin 3-5 days before the surgery**. **Heparin is usually started instead**. This is called "**Heparin Bridging**".

	◙ After Stopping Warfarin (3-5 days before surgery), surgery can take place when INR is < 1.5. ◙ Heparin is more easily and rapidly reversed. ◙ Resume Warfarin at the evening of the operation day when INR at the therapeutic levels (Not Always).
Key 42	**◙ A Quick Recap on Mode of Inheritance:** √ **Hemophilia** → X-linked Recessive. √ **G6PD deficiency** → X-linked Recessive. √ **VWD** → Mostly Autosomal Dominant. √ **Hereditary Spherocytosis** → Mostly Autosomal Dominant. √ **Thalassemia** → Autosomal Recessive. √ **Sickle Cell Anemia** → Autosomal Recessive. **Chance of Inheritance to Children** ◙ Autosomal **Recessive** Conditions: (25% if **both parents** are **carriers**) ◙ Autosomal **Dominant** Conditions: (50% if **One parent** is **affected**) ◙ X-linked **Recessive** Conditions: (**Male**: 50% if **mother** is **carrier**)

	◙ Others -from the genetic chapter- √ **Cystic Fibrosis**, **Congenital Adrenal Hyperplasia** → **Autosomal Recessive**. √ **ADPKD**, **BRCA gene**, **Neurofibromatosis**, **Huntington's** → **Autosomal Dominant**. √ **Duchenne Muscular Dystrophy** (**DMD**) → **X-linked Recessive**. • Alport Syndrome → X-linked (0% to pass from a father to a male child)
Key 43	• **Parvovirus B19 (Aplastic Crisis)** → Severely **Low Hb** and **Low Reticulocytes**. • **Splenic Sequestration Crisis** → Severely **Low Hb**, But **High Reticulocytes**. ♦ **Parvovirus B19** → **Sickle Cell Anemia** or **H. Spherocytosis**. ♦ **EBV Lymphomas** → **Burkitt's Lymphoma** or **Hodgkin's Lymphoma**. ♦ **AIDS (HIV)-related Lymphomas** → **Non-Hodgkin's Lymphoma** (Diffuse large B cell) followed by (Burkitt's lymphoma).
Key 44	**Complications (Crises) of Sickle Cell Anemia** **◙ Thrombotic (Vaso-occlusive) Crisis:** • The commonest complication of SCA. • Sickle-shaped RBCs act as clots and cause occlusion of small blood vessels → Ischemia-like features (eg, pain).

- Common Scenarios:

√ Mesenteric Ischemia (Acute Abdomen).

√ Avascular Necrosis (eg, femoral head).

◙ Splenic Sequestration Crisis:

- Sudden Enlargement of Spleen. (Pooling of RBCs)
- Very low Hb.
- **High** Reticulocytes.
- If recurrent → Splenectomy.

◙ Aplastic Crisis:

- Commonly due to (**Parvovirus B19**).

If you see Parvovirus → Aplastic Crisis.

- Very low Hb. (Transient stoppage of erythropoiesis → everything is low).
- Very **low** Reticulocytes.

◙ Hemolytic Crisis: (Rare).

Management of Pain in Sickle Cell Anemia Crisis (Chest Pain):

- A bolus of strong opioids (usually morphine).
- If the pain persists after reassessment:

→ Another bolus of morphine is given.

Notes:

√ Ibuprofen (NSAIDs) can be also given.

√ Oxycodone can be considered if morphine is not tolerated (as an alternative and not as an additional medication).

√ Pethidine should be avoided in sickle cell anemia (risk of seizures).

√ If repeated boluses are needed within 2 hours:

Consider → Patient controlled analgesia.

Example,

A 19 YO ♂ known case of Sickle Cell Anemia presents with pallor, Shortness of breath, lethargy and headache. For the past week, he has been having flu-like symptoms. He also complains of joint aches on his hands, wrists, knees and ankles for the previous few days. His Hb is 56 g/L. Doctors suspected parvovirus B19 infection and sent specific IgM and IgG antibodies to Parvovirus B19.

The likely Diagnosis → **Aplastic Crisis**.

√ Once you see parvovirus B19 in SCA or Hereditary Spherocytosis

→ Aplastic Crisis.

Key 45

Beta Thalassemia Major (Autosomal Recessive)

- Microcytic anemia.
- Marked Pallor
- Mild Jaundice
- Has to receive Blood Transfusion **frequently**
- Hepatosplenomegaly
- Frontal Bone Bossing (Skull Bossing)
- Frequent blood transfusions → Iron overload → Endocrinopathy e.g. DM.

◙ Rx:

√ **Lifelong Blood Transfusion** (maintain Hb > 9.5).

√ **Iron Chelating Agents** (e.g., **Deferoxamine** "Desferal" SC twice a week)

- Remember, beta thalassemia **Major** starts since infancy and results in failure to thrive, vomiting feeds.

	And in adulthood if untreated, it can lead to frontal bossing and hepatosplenomegaly. •B thalassemia **Minor** (or thalassemia trait) is usually asymptomatic during childhood. However, in adulthood it may manifest as microcytic anemia with lethargy and mild anemia.
Key 46	A child presents with **epistaxis**. His **labs are normal** (Platelets, PT, PTT, Bleeding Time). √ The likely cause → **Anatomical Defect** or **Trauma**.
Key 47	**Remember that:** ♦ The **CHA2DS2-VASc score** is used to determine **the need to anticoagulants** in a patient who has **atrial fibrillation**. ♦ The **ABCD2 score** (Prognostic) is used to **identify the risk of stroke in patients who have had a suspected TIA.**
Key 48	**In a Patient with Atrial Fibrillation,** **→ We Calculate the CHA2DS2-VASc Score:**

Abbreviation	Risk Factor	Points
C	Congestive Heart Failure (LVEF<40%)	1
H	Hypertension	1
A	Age≥75 years	2
D	Diabetes Mellitus	1
S	Stroke/TIA or systemic embolism	2
V	Vascular Disease	1
A	Age 65-74 years	1
Sc	Sex category (female)	1

♠ Give Warfarin or DOAC (**D**irect-Acting **O**ral **A**nti**C**oagulants, such as **Apixaban**, **Rivaroxaban**, **Edoxaban**, **Dabigatran**) To →

◙ **All** patients with score **≥ 2**.

◙ Consider giving Warfarin or DOAC to **Men** whose scores **≥ 1.**

Advantages of DOAC:

- No need for INR Monitoring,
- Faster Onset of Action (2-4 hours),
- Reduces the risk of intracranial Hemorrhage.

	Disadvantages of DOAC: - No Antidote - Require strict compliance by the patients. ***Note, it is important to remember DOAC Medications! They are asked in the exam in a stem which describes a patient with Atrial Fibrillation. We either give Warfarin or DOAC (e.g. Apixaban) as a long-term anticoagulant.***
Key 49	After C-Section, a woman develops swelling of her entire left leg starting at the level just above the inguinal ligament. She also has Back and Buttock pain. The likely cause → **Common iliac VENOUS thrombosis**. **√ DVT is common in pregnancy and Post C-Section.** √ The Swelling in "**iliac**" **VEIN thrombosis** begins **ABOVE** the level of inguinal Ligament ± Back and Buttock pain. √ The Swelling in "**Femoral**" **VEIN thrombosis** will begin **BELOW** the level of inguinal Ligament. √ **Arterial Occlusion** does not present with Swelling like in this stem, it rather presents with the known (**6P features of Acute Limb Ischemia**) → **P**ain (Sudden), **P**allor, **P**ulselessness, **P**aralysis, **P**araesthesia (Numbness), **P**erishing cold.

Key 50	**The Diagnostic Test in Lymphoma → LN Biopsy.**
Key 51	**ALL (Acute Lymph. Leukemia) diagnostic test:** → **Bone marrow biopsy**
Key 52	**An elderly ♀ presents with chest infection and thus was started with clarithromycin. Her Hx includes, taking Carbamazepine for trigeminal neuralgia, taking Warfarin for mechanical valve replacement, taking Bisoprolol, Amlodipine and Atorvastatin. Her INR was found to be 1.4 (The target for mechanical valve replacement is 3-4). What is the causative drug for this low INR?** The answer → **Carbamazepine** ◙ **Carbamazepine** is P450 enzyme **inducer**; thus, it will **decrease** the anticoagulant effect of Warfarin and therefore leads to **low** INR.
Key 53	**An elderly patient with Hx of Atrial Fibrillation on Warfarin was found to have INR of 7 He is on Warfarin. He has epistaxis (Minor bleeding). What should be done at the anticoagulant clinic?** → **Stop Warfarin, Repeat INR the Next day**.

	(**INR 5-8 with or without minor bleeding**) → STOP WARFARIN and Restart when INR is < 5. Epistaxis is a minor bleeding. (Note that if INR was > 8 ± minor bleeding, we would give vitamin K1)
Key 54	**A patient presents with jaundice, dark urine and abdominal pain. After investigations → Heinz bodies and bite cells were found.** → **G6PD**
Key 55	**A patient has started taking anti-malarial medications after returning from abroad. He then develops mild jaundice, dark urine and tender right abdomen and palpable liver.** → **Hemolytic Anemia** (likely **G6PD**).
Key 56	**A patient presents with Bloody Diarrhea followed by renal function tests impairment.** → **HUS (Hemolytic Uremic Syndrome)**

Important Table

Hematuria + HTN	Polycystic Kidney Disease (ADPKD)	Ultrasound
Hematuria + Hemoptysis	Goodpasture Syndrome	Anti-GBM Abs
Hematuria + Hemoptysis + Nasal/Sinus problems	Wegener's (Granulomatosis with Polyangiitis)	c-ANCA
Hematuria/ Renal function impairment + Bloody diarrhea	Hemolytic Uremic Syndrome (HUS)	www.Plab1keys.com

Key 57	**A woman presents with irritability, Peripheral Paraesthesia, numbness, Impaired proprioception and low Hb.** → **Vitamin B12 Deficiency**.
Key 58	**10 YO boy presents with a low-grade fever and macular rash especially on the back of the legs following an upper respiratory tract infection. A few hours**

later, these macules have turned into purpuric lesions that do not blanch on glass test. The boy also complains of joint stiffness and headache.

Hb (124 g/L) ▌WBC (3.3 X 10^9/L) ▌Platelets (219 X 10^9/L).

The Likely Dx → **Henoch-Schonlein Purpura (HSP)**

Note that Hb, WBCs, and platelets are normal.

Please note that if a patient presents with similar features but with LOW PLATELETS and normal Hb and WBCs, the answer would be → Idiopathic Thrombocytopenic Purpura (Explained Later in Key 17).

Note, renal impairment is rare but can occur.

REMEMBER

- **Haemophilia** (X-linked recessive, so the affected individual is a boy mainly)

→ ↑ **PTT** + (Bleeding into muscles or joints or easily bleeds).

- **Henoch-Schonlein Purpura**

HSP → **PAAN**: non-blanching **P**urpura ± **A**rthralgia, **A**bdominal pain, **N**ephropathy (Hematuria, Proteinuria) "not always".

	• Purpura is **non-blanching** and mainly on the **buttocks** and **Lower Limbs**. • Precipitated by **URTI – Sore Throat**. • All Blood Results are **NORMAL** "Normal Hb, WBCs and Platelets". • However, there might be **↑ ESR/ IgA/ Creatinine** • **Idiopathic Thrombocytopenic Purpura (ITP)** **Isolated Thrombocytopenia** (low platelets) has to be given in a stem.
Key 59	**A man presents with night sweats, fever and lymphadenopathy.** → **Lymphoma**. --- **Manifestations of Lymphoma** √ **Painless**, **Rubbery** slowly progressive Peripheral **lymphadenopathy**. "**The commonest**". √ Systemic manifestations → fever, malaise, **fatigue**, **weight loss** (Late stage). √ **B Symptoms** → **Unintended Weight Loss** ▌**Unexplained Fever** ▌**Night Sweats**. √ **Splenomegaly**, **Hepatomegaly**. √ BM is frequently involved → **Pancytopenia** → Anemia, Infections, Bleeding.

Key 60

◙ Hx of GI issue, **Diarrhea** → turns **Bloody** → **Renal Failure** (**Hematuria**, **proteinuria**…etc).

± **Features of Anemia** (e.g. Pallor, Fatigue) **± Low Platelets**

→ **Hemolytic Uremic Syndrome** (especially in young people).

Hematuria + HTN	Polycystic Kidney Disease (ADPKD)	Ultrasound
Hematuria + Hemoptysis	Goodpasture Syndrome	Anti-GBM Abs
Hematuria + Hemoptysis + Nasal/Sinus problems	Wegener's (Granulomatosis with Polyangiitis)	c-ANCA
Hematuria + Bloody Diarrhea (after GI infection)	Hemolytic Uremic Syndrome (HUS)	www.Plab1keys.com

Key 61

60 YO ♂ presents with Hx of Back and Ribs pain + being Thirsty + Tiredness.

	Hb is 90 g/L (low) ▌ Ca^{++} is 4 (high) ▌ ALP is 115 (normal) ▌ ESR is 88 ▌ eGFR is 45 (low). ◙ The likely Dx → **Multiple Myeloma**. ◙ The cell type to be found in BM → **Plasma Cells**. ◙ The Most **definitive Diagnostic** Test → **Bone Marrow Biopsy**. √ ◙ The likely finding on blood film → **Rouleaux Formation**. √ Anemia is the commonest laboratory finding in MM. √ Renal Impairment presents in 50% of MM cases. √ In MM, High Calcium but normal ALP.
Key 62	◙ Old (> 60 YO), usually no splenomegaly, **smudge cells**, Cervical LNs, ↑↑**Mature Lymphocytes**. → CLL
Key 63	◙ **The target INR in most cases "Including Warfarin intake for AF, DVT"** → **2-3** ◙ The target INR in **mechanical valve replacement** "**Metallic Valve**" → **3-4**

Key 64	◙ A man on warfarin fell and presents with confusion. His INR was found to be 6.1 What should be done? We suspect he has an intra-cranial hemorrhage (namely: **subdural hematoma**) Elderly + on warfarin + Hx of fall + presents with confusion/ headache Suspect → **Subdural hematoma** (In Neurology chapter). Since **intracranial hemorrhage** is a **Major Bleeding**, we give → **Prothrombin complex concentrate**.
Key 65	◙ An elderly man with dementia, recurrent visits to the hospital for **bruises** in the **face**, **head** and **forearms**. → Suspect "**non-accidental injury**". Someone is abusing this old man as the bruises are in suspicious sites. If the cause was "recurrent falls" for instance, the bruises would have been over the hip, knee or shoulder joints, not in the face!
Key 66	◙ vegetarian with megaloblastic anemia (↑ MCV) → **Vitamin B 12 Deficiency**.

Key 67	◙ **A child with swollen lymph nodes. Which is the <u>best</u> diagnostic tool.** → **Lymph node biopsy**
Key 68	**A 60-year-old woman who is to have a blood transfusion had pre-transfusion vitals of T=37.3, Pulse rate 114bpm, Spo2 96% and BP 114/73mmhg** **4 hours post transfusion, she started feeling unwell and her vitals were T 38.4 Pulse rate 94 spo2 96% BP 120/85mg** **What is the most likely diagnosis?** A. Acute Hemolytic Transfusion reaction B. Anaphylaxis C. Bacterial contamination D. **Febrile Non-hemolytic Transfusion Reaction** E. Normal reaction **Febrile Non-hemolytic Transfusion Reaction** (FNHTR) √ ↑ in Temp. of around 1 – 2°C during or after blood transfusion. √ Occurs during transfusion or up to 4 hours after transfusion.

√ **Rx**:

• Stop transfusion while continuing to give normal saline.

• Give Paracetamol.

• Resume blood transfusion when the symptoms and fever subside.

• Observe the patient for 15-30 minutes

◙ FNHTR "Febrile Non-Haemolytic Transfusion Reaction":

♦ Fever of > 38

♦ ↑ in Temp of at least 1 degree up to 2 degrees from pre-transfusion temperature.

♦ Other vitals are within normal with no significant changes from Pre-transfusion vitals.

◙ Why not Acute Hemolytic Transfusion Reaction (AHTR)?

	AHTR can be fatal. It starts **within minutes of transfusion.** Some S&S include: √ Fever, √ Hypotension/ Shock, √ Pain at the transfusion site, ± DIC (↑ Bleeding), ± Haemoglobinuria/ Hemoglobinemia, ± Feeling of impending doom "death".
Key 69	**Sore legs "Painful legs"** + **Swollen Varicose Veins** from the mid-thigh to the ankle → **Superficial Thrombophlebitis**. → Give **NSAIDs** "To relieve the pain- sore- ". ***Example***, You are reviewing a female patient who has undergone Laparoscopic cholecystectomy a few hours ago. You notice that there is a sore leg with swollen varicose veins extending from the left mid-thigh to the ankle. There is no calf tenderness or calf swelling. ♦ Since there is no calf tenderness or swelling → Likely Not DVT. ♦ Sore "Inflamed/painful" + Varicose Veins → Superficial Thrombophlebitis.

	The next step → **Relieve the soreness by Prescribing → NSAIDs**. ***Never Reassure and leave a patient in pain. At least, relieve his pain!*** *Note,* **D-dimers** should not be requested post-op as they are **usually elevated after surgery.** D-Dimers are high in DVT and in Superficial Thrombophlebitis. Thus, pointless in this scenario.
Key 70	**A woman who started chemotherapy yesterday for Burkitt's lymphoma. Urinary output reduced to 40mls in last 12hours. Lab tests on admission were normal.** **Lab results now show raised K, Raised Urea, Raised creatinine.** **What test would point to the cause of her deterioration**? a. esr level b. C reactive protein c creatinine kinase d **Urate level** e phosphate level

	Tumor Lysis Syndrome → **UK Pc** HyperUricemia (↑ **Uric Acid** "Also called **serum Urate**) → Gout. HyperKalemia (↑ K^+ "**Potassium**") HyperPhosphatemia (↑ **Phosphate**) Hypocalcemia. (↓ **Calcium**). √ It occurs mainly in Leukemia (Especially **ALL**) and Lymphoma (Particularly **Burkitt's Lymphoma**) after initiating **Chemotherapy**. √ Chemotherapy, Radiotherapy, Surgery → **Rapid Lysis of Tumour Cells** → Excessive amounts of Uric acid "Urate", Potassium and Phosphate are released into the blood.
Key 71	**A 57-year-old man presents with lethargy and he looks pale. Blood pressure is 150/100.** **Urinalysis: Blood +++, Protein +++, Creatinine: Elevated, Ca is high** **Other tests normal. What's the appropriate investigation?** a. **Urine for Bence Jones protein** b. Renal Ultrasound c. Cystoscopy d. Blood culture

	e. 24hour urine collection **Pale and lethargy → Anemia** **Renal Failure** **Hypercalcemia** **Others (not mentioned here): Bone pain, Recurrent infections** Think → **Multiple Myeloma** ◙ Urine electrophoresis → **Bence Jones Protein.** ◙ The cell type to be found in BM → **Plasma Cells**. ◙ The Diagnostic Test → **Bone Marrow Biopsy**. ◙ The likely finding on blood film → **Rouleaux Formation.**
Key 72	**A 68-year-old woman with a painless lump in her anterior neck, not mobile and was otherwise fine. She also has swelling of her ant cervical nodes, supraclavicular nodes, axillary nodes and inguinal nodes all bilaterally, WBC 27*10^9 (High), Lymphocytes 21*10^9 (High), Other investigations were mostly normal. Blood film revealed lymphocytes with smudge cells.** A. ALL

B. **CLL (Chronic Lymphocytic Leukemia).**

C. Hodgkin's lymphoma

D. Burkitt's

e. CML

◙ Old (> 60 YO), usually no splenomegaly, **smudge cells**, Cervical LNs, ↑↑**Mature Lymphocytes**.

→ CLL

ALL	Child (Up to 15 YO), **Pancytopenia**, **Blast cells**.
AML	Adult (20-30 YO), **Auer rods**, **Blast cells**.
CML	Middle age (40-50 YO), Massive Splenomegaly, Philadelphia chromosome, **Granulocytes** (Neutrophils, basophils eosinophils) **without blast cell, in all stages of maturation** (i.e. myelocytes, metamyelocytes…)
CLL	Old (> 60 YO), usually no splenomegaly, **smudge cells**, Cervical LNs, **Mature Lymphocytes**.

Key 73	**A 5-year-old girl with 5 days history of bloody diarrhoea and dehydration. Blood culture shows E. coli**

	Na+ low, K+ high, Creatinine high, Urea high, Calcium Normal, Bicarbonate low. What is the likely diagnosis? a. **Acute kidney injury** b. Addison's c. Renal tubular acidosis √ This is a classic case of HUS (Hemolytic-Uremic Syndrome). √ **HUS** is the **most common** cause of **acute kidney injury** in **children** and is increasingly recognized in adults.
Key 74	**60 YO ♀ presents with tiredness and easy fatigability. She is mildly jaundiced.** **Labs are as follows:** **Hb 87 g/L ▌MCV 98 fL (normal: 76-96) ▌WBCs 8 ▌Bilirubin 40 (high)** **ALT, AST, ALP and Gamma Glutamyl Transferase are normal.** **Peripheral Blood Smear → Spherocytes.** ◙ The appropriate Investigation → **Direct Antiglobulin (Direct Coomb) Test**. **Anemia + jaundice + High bilirubin → hemolysis.**

• **Spherocytes** → Hereditary Spherocytosis**?** Nope! Not necessarily! Spherocytes can be seen in both Hereditary Spherocytosis and Autoimmune Hemolytic Anemia. To Differentiate → **Direct Coomb Test**.

In this scenario, although we suspect hereditary spherocytosis, Direct Coomb "Direct antiglobulin" test would differentiate the cause of the hemolysis. This is because it will be +ve in Autoimmune Hemolytic Anemia, and -ve in Hereditary Spherocytosis.

Osmotic Fragility Test is **positive** in both **Hereditary Spherocytosis** and **Autoimmune hemolytic anemia**.

Direct coomb "antiglobulin" test is **positive** in Autoimmune hemolytic anemia and **negative** in Hereditary Spherocytosis.

Thus, Direct coomb is more appropriate as it can differentiate the 2 cases.

Additional Important Notes:

◙ Direct Coomb Test (Direct Anti-globulin test):

√ It detects antibodies on the **RBCs Surfaces**.

√ Used for → **Autoimmune Haemolytic Anemia** (AHA).

◙ Indirect Coomb Test (Indirect Anti-globulin test):

√ It detects antibodies in the **Serum**.

	√ 2 Major uses: • **Blood Transfusion Preparation** (**Cross-matching**). • **Antenatal antibody screening** → Screening a pregnant ♀ for **IgG** antibodies that can cross the placenta and cause hemolysis in fetal blood. ◙ **Osmotic Fragility test** → Hereditary Spherocytosis.
Key 75	**Patient with intracranial bleeding. INR is 4.6. He was given IV vitamin K. What is next to be given?** A. Fresh Frozen Plasma B. **Prothrombin Complex Concentrate (PCC)** C. Tranexamic acid D. IVF Intracranial Bleeding is a major bleeding. So, we should give both Vit K and PCC.
Key 76	**A woman presents with lethargy, Raised MCV 108, Low Hb and tingling sensations over fingers. Best investigation?** → **Vit B12 and Folic Acid** (Classical Picture of Vit B12 Def.)

	◙ **Remember the features of Vitamin B12 Deficiency:** - **Peripheral paraesthesia**. - **Impaired position and vibration** (**proprioception**) **sense**. - **Dementia** → loss of memory, difficulties with thinking. - If untreated → permanent **Ataxia**.
Key 77	**According to the recent guidelines (2019),** **√ ABCD2 score which was used in the past to assess the risk of a future stroke in the following 7 days after having a TIA is NOT advised now.** **√ Therefore, ~~ABCD2 score~~ would not be a correct answer in the exams.** **However, CHA2DS2VASc score is still used to assess the need for anticoagulants (such as Warfarin, DOAC: apixaban, dabigatran) in patients with atrial fibrillation to avoid future stroke.**
Key 78	**Post-op patients who are expected to remain immobilized for a period of time need to be given:** → **Prophylactic dose of Low Molecular Weight Heparin e.g. enoxaparin.** √ A prophylactic dose, not a treatment does.

	√ This is to help prevent DVT, Pulmonary embolism …etc.
Key 79	**Important Update on DVT Management:** Now, treatment doses of **DOACs** (e.g. **Apixaban**, **Rivaroxaban**) have become **superior to Low Molecular Weight Heparin** as anticoagulants. Thus, in the exam, if both treatment dose of apixaban/rivaroxaban and low molecular weight heparin are within the options, pick the one with rivaroxaban/apixaban. ◙ **This is to say, in suspected DVT (calf swelling, pain, pitting edema)** **→ D-dimer, therapeutic dose of rivaroxaban, Leg Ultrasound in 24 hours**. ◙ **What if the patient is already on the maximum dose of rivaroxaban (anticoagulant) and presents with calf pain, edema, swelling?** In this specific case, he is already on maximum dose anticoagulant, we **request D-dimer and arrange leg U/S in 24 hours**. After which, we may put him on different anticoagulants such as a combination of warfarin and LMWH. ◙ **What if these are 2 separate options (either D-dimer or U/S)?** → Pick **U/S of the legs** as long as the DVT is likely.

◙ What if DVT is unlikely?

→ D-dimer may be enough.

◙ When to say DVT is likely or Unlikely?

→ Well's score of 2 or more = DVT is likely.

→ Well's score of 1 or 0 = DVT is unlikely.

See the table below (Well's Criteria for DVT):

Clinical Feature	Points
Active cancer (on treatment, treated in the last 6 months or palliative)	1
Paralysis, paresis or plaster immobilisation of the lower limb	1
Bedridden for 3 days or more, or major surgery in the past 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf Swelling 3 cm larger than the symptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previous DVT	1
Alternative diagnosis is at least as likely as DVT	-2
Clinical probability simplified score	Points
DVT likely	2 points or more
DVT unlikely	1 point or less

	Note that Ultrasound of the affected leg is preferred to be done in **4 hours**. **However**, in most parts of the UK, this is usually not possible. Therefore, we request D-Dimer, start treatment dose of DOACs (e.g. apixaban or rivaroxaban) and arrange U/S of the leg in 24 hours. ***√ Note that we start with a treatment dose, not a prophylactic dose!*** ***√ Note that a prophylactic dose is started post-op to prevent venous thromboembolism. But once we have manifestations, we start a treatment dose (increase the dose) even prior to reaching a diagnosis!***
Key 80	**High MCV + Low Hb → Megaloblastic anemia** Either **vitamin B12 deficiency** or **Folate deficiency** or Both. **For Megaloblastic Anemia (low Hb, high MCV):** **If the question asks about what is the best option test to specify the cause of this megaloblastic anemia, you have to choose either (Vitamin B12 assay) or (serum or red cell Folate). So, what to pick?** **√** If there are: **Peripheral Paraesthesia "Pins and Needles sensation"**, Loss of position and Vibration sense, Ataxia, confusion. → Vitamin B12 deficiency. **√** If the patient does not eat vegetables and eat meat → Folate deficiency.

	✓ If the patient is vegan (does not eat meat and dairy products) → Vitamin B12 deficiency. ✓ If the patient depends on microwavable food, canned food, with no vegetables → Folate deficiency. *The key is to know that Vit.B12 is present in fish, meat, and dairy products while folic acid is present in vegetables.* Note also that Folic acid stores in the body last for 4 months or less, while vitamin B12 store may last for up to 4 years!
Key 81	• **Patients on warfarin need to** → **Stop warfarin 5 days before surgery.** • **Patients on DOACs (eg, apixaban) need to** → **Stop warfarin 24 hours before surgery (if low bleeding risk surgery).** → **Stop warfarin 48 hours before surgery (if high bleeding risk surgery).**
Key 82	**Scenario:** A 3 YO child returned recently from India to the UK. He is lethargic and pale. His main diet is milk, with little to none of solid food. His lab

results show low Hb, low MCV, low MCHC. What is the most likely diagnosis?

A • Alpha thalassemia major.

B • Beta thalassemia trait.

C • Iron deficiency anemia.

D • Folate deficiency.

E • Vitamin B 12 deficiency.

The answer:

→ **Iron deficiency anemia.**

"**Milk decreases the absorption of iron**"

√ Alpha thalassemia major is usually fatal and causes hydrops fetalis. The baby would not survive gestation.

√ Beta thalassemia trait is asymptomatic. It can result in lethargy and mild anemia in adulthood (not childhood or infancy).

√ Folic acid and B12 deficiency cause Macrocytic anemia, however, the stem gives labs of microcytic anemia.

Key 83	**A 77 YO man comes to the GP complaining of weight loss and fevers over the past 4 months. O/E, several cervical LNs are enlarged and painless. Blood results show: low Hb, high WBCs. LNs biopsy shows bi-nucleated cells with prominent nucleoli.** The likely Dx → **Hodgkin's Lymphoma**. **Hodgkin's:** √ Bimodal: < 25 YO or > 55 YO. √ The diagnostic feature given here is the bi-nucleated cells with prominent nucleoli which represent Reed Sternberg cells that are characteristic for Hodgkin's lymphoma.
Key 84	**A 77 YO man comes to the GP complaining of weight loss and fevers over the past 4 months. O/E, several cervical LNs are enlarged and painless. Blood results show: low Hb, high WBCs. LNs biopsy shows monomorphic small irregular B lymphocytes.** The likely Dx → **Non-Hodgkin's Lymphoma**. • The given features are seen in lymphoma: Weight loss – loss of appetite – fever – Painless cervical lymphadenopathy • Monomorphic small irregular B lymphocytes can be seen in **non**-Hodgkin's.

• If the biopsy showed cells **other than** Reed Sternberg cells (multi- or bi-nucleated cells with prominent nucleoli), it is likely non-Hodgkin's.

This is to say: in Hodgkin's lymphoma, there are Reed Sternberg cells (which are bi- or multinucleated cells with prominent nucleoli. If these cells are not seen, but other cells (eg, monomorphic, small, irregular B lymphocytes) and the symptoms go with lymphoma, then think of **non**-Hodgkin's lymphoma.

If the same scenario is given but without mentioning that LN biopsy has been done and asks you about the most appropriate (or diagnostic) **investigation**?

→ Lymph node biopsy. (important)

Manifestations of Lymphoma

√ **Painless, Rubbery** slowly progressive Peripheral **lymphadenopathy**. "**The commonest**".

√ Systemic manifestations → fever, malaise, **fatigue**, **weight loss** (Late stage).

√ **B Symptoms** → **Unintended Weight Loss** ▌**Unexplained Fever** ▌**Night Sweats**

√ **Splenomegaly**, **Hepatomegaly**.

√ BM is frequently involved → **Pancytopenia** → Anemia, Infections, Bleeding.

√ **Excisional biopsy** is essential.

Key 85	• [**After surgery**], if the patient will be immobile for a while, it is beneficial to → **Wear Compression Stockings** to prevent DVT. **HOWEVER**: • If the patient is admitted with [**Acute Stroke**], to prevent DVT, use: → **Intermittent pneumatic compression**. Be careful, **intermittent pneumatic compression** is preferred if the patient is admitted with **acute stroke**! Elastic compression stockings are not beneficial in acute stroke; they are helpful in general surgeries. Both are used to prevent venous thromboembolism. Both were asked before. • **Prophylactic** dose "**not** treatment dose" of LMWH (eg, enoxaparin) or direct oral anticoagulants (DOAC) (eg, apixaban) can also reduce the risk of DVT. Careful! • **Treatment** dose is given if there is a **suspected or confirmed** case of DVT or Pulmonary embolism. • But for general people who will be immobile after surgery → Compression stockings, + can use "**prophylactic dose**" of LMWH or DOAC if no contraindications.
Key 86	**A 33 YO man has been investigated for lethargy that started a few years ago. His hemoglobin is 9. His MCV and MCHC are low. However, his ferritin**

and total iron binding capacity are normal. He was diagnosed with crohn's disease a few months ago. What is the likely Dx?

(Anemia of chronic disease /Iron deficiency anemia / beta thalassemia major / beta thalassemia minor (beta thalassemia trait))?

This is a case of microcytic anemia (low MCV and low MCHC).

All given options are microcytic anaemias (except sideroblastic anemia which can be normocytic or microcytic or macrocytic).

• Since TIBC and ferritin are normal → it is **NOT iron deficiency anemia** and also **not anemia of chronic disease**.

• Remember, beta thalassemia **Major** starts since infancy and results in failure to thrive, vomiting feeds.

And in adulthood if untreated it can lead to frontal bossing and hepatosplenomegaly.

• Here, this has started in adulthood with lethargy and mild anemia, which is compliance with beta thalassemia **Minor** (or beta thalassemia **trait**).

• **Sideroblastic anemia** (can sometimes be microcytic): the bone marrow produces ringed sideroblasts rather than healthy red blood cells. In sideroblastic anemia, the body has iron available but cannot incorporate it into hemoglobin, which red blood cells need in order to transport oxygen efficiently.

	Here; no mention of bone marrow di"ease' Also, serum iron and ferritin are usually (↑) in sideroblastic anemia. Here, they are normal.
Key 87	**A 40 YO man who has had bariatric surgery 3 years ago has been feeling lethargic in the past few months. His labs show Hb of 9, high MCV, normal iron studies. What is the likely diagnosis?** → **Vitamin B12 deficiency anemia** • Since MCV is high → Macrocytic or megaloblastic anemia → Either vitamin B12 or folate deficiency. • Since the patient has had bariatric surgery (this could include gastric bypass or sleeve gastrectomy): Gastrectomy → Loss of the intrinsic factors in the stomach → impaired Vitamin B12 (Cobalamin) absorption → Vitamin B12 deficiency. • **Rx** → Intramuscular Hydroxocobalamin (vit b12) injections for life. Vitamin B 12 tablet are of no help as the problem is in the absorption (decreased absorption due to gastrectomy). Give it IM.

Key 88	Patients with **DVT** or **Pulmonary embolism** **DO NOT NEED** to inform DVLA and they can drive (no restrictions on driving for DVT or PE patients) as long as they haven't experienced loss of consciousness and can move their legs.
Key 89	**Chronic alcohol consumer + Gum bleeding, Petechiae** **Think** → **Vitamin K deficiency**. Especially if the issue is only for a few weeks. Chronic alcohol consuming can cause depletion of both vitamin **K** and **C**. However, vitamin K deficiency is a more common cause of bleeding in this case. Also, in vitamin K deficiency, serum PT would be low. **Important**: If there were additional things in the stem that describe **scurvy** "**vitamin C deficiency**" such as: Being an elderly, neglected and living alone "not eating fresh fruits" Pallor "anemia is a feature of vitamin C deficiency" Hypertrophic gums **Then Pick** → **Vitamin C deficiency**. Especially if the issue is for long eg, months. In short, **vitamin K deficiency** is a faster and a more common cause for bleeding in alcohol abusers. However, **vitamin C deficiency** can also occur in alcoholics especially of long time "as the total depletion of vitamin C storage takes more time than that of vitamin K depletion" and there will be other features besides bleeding that indicate vitamin C deficiency such as enlarged bleeding and friable gums, pallor, being elderly, neglected and malnourished.

90

Important Points to Remember on Ischemic Stroke

• The antihypertensive of choice in patients with diabetes mellitus is

→ ACE inhibitors (eg, ramipril).

• In patients with a history of ischemic stroke, the long-term management to prevent further stroke (2ry prevention of ischemic stroke) is as follows:

√ Control Blood Pressure.

Remember, if he has diabetes, pick or add ACEi eg, ramipril.

√ Statins (for All patients regardless of their cholesterol baseline level).

√ Ani-platelets (or) **Anti-coagulation**: (Based on presence or absence of AF):

· If there is Atrial Fibrillation → Anticoagulants: Warfarin [or] DOAC (Dabigatran/ Apixaban/ Rivaroxaban/ Edoxaban). DOAC is now preferred.

(Warfarin is almost obsolete nowadays. DOAC is recommended instead).

· If No Atrial Fibrillation → Antiplatelets: Clopidogrel 75 mg OD.

Important: What if a patient with a history of stroke is already on warfarin and presents with a new onset atrial fibrillation?

Since he is already on an anticoagulant, he should continue on warfarin and should not be switched to DOAC (eg, Edoxaban) unless his INR is abnormal.

Scenario (1) that tests the above notes (important).

A 65 YO man presents for medication review. He has a history of ischemic stroke a few months ago. His medical background includes atrial fibrillation, hypertension and type 2 diabetes mellitus. His ECG still shows arterial fibrillation. He is on warfarin, lercanidipine (CCB), atorvastatin, and metformin. His current blood pressure is 160/100. What is the most appropriate action?

A) Switch warfarin to Edoxaban (DOAC).

B) Continue warfarin and add clopidogrel.

C) Stop lercanidipine and start ramipril.

D) Continue lercanidipine and add ramipril.

E) Continue lercanidipine and add bendroflumethiazide.

The right answer is (D): continue lercanidipine (CCB) and add ramipril (ACEi).

• Since he is **diabetic**, **ACEi** is of choice to control HTN.

• Since he is already on an antihypertensive (which is lercanidipine; a calcium channel blocker) and **his hypertension is still uncontrolled**, go to step 2 and add a second antihypertensive (**ACE inhibitor** eg, **ramipril**).

• We **do not shift** from warfarin to DOAC unless his INR is not normal. Here, no mention of INR. Thus, continue on warfarin (option A is wrong).

• Since he has AF, an anticoagulant (eg, warfarin, DOAC) is given; Not an antiplatelet (eg, clopidogrel).

Scenario (2) that tests the above notes (important).

A 61 YO man presents for medication review. He has a history of ischemic stroke a few months ago. His medical background includes hypertension and type 2 diabetes mellitus. His ECG now shows arterial fibrillation. He is on clopidogrel, amlodipine, atorvastatin, and metformin. What is the most appropriate action?

A) Switch amlodipine to ramipril.

B) Continue clopidogrel and add apixaban.

C) Stop clopidogrel and start edoxaban.

D) Continue amlodipine and add ramipril.

E) Continue amlodipine and add bendroflumethiazide.

The right answer is ©: Stop clopidogrel and start a DOAC eg, edoxaban.

• He did not have atrial fibrillation before, that's why he was on clopidogrel (and not warfarin or DOAC).

• Since he is now having atrial fibrillation, switch clopidogrel to an anticoagulant such as warfarin or DOAC (eg, edoxaban, apixaban). DOAC is preferred over warfarin.

• His blood pressure is not mentioned so we assume it is controlled and therefore no need to add an additional antihypertensive (even if he is diabetic, he is already on amlodipine and controlled).

Key 91	**When is Blood Transfusion Indicated?** • If Hb **< 70 g/L** (either symptomatic or not). • If Hb **< 80 g/L** (+) symptoms of anemia (eg, fatigue, tachycardia, pallor). • If Hb **< 90 g/L** (+) there is a known cardiovascular disease. Very low hemoglobin puts patients at risk of arrhythmia and heart failure. **Example**: A 35 YO woman with history of menorrhagia presented with fatigue. Her MCV is low and her hemoglobin is 68 g/L. What should be done? RBC transfusion (or) IV iron supplements (or) Oral ferrous sulphate? • Her low MCV and low Hb + Hx of menorrhagia → Iron deficiency anemia. • Since Hb <70 g/L → RBC transfusion (she is also symptomatic; fatigued)! **Note**: 70 g/L is the same as 7 g/dL (but the unit is different).
Key 92	One of the reasons of iron deficiency anemia that needs to be investigated for if the cause of IDA is unknow is → Celiac disease (tissue transglutaminase IgA).
Key 93	**Do Not Mix Things Up:**

	• [**After surgery**], if the patient will be immobile for a while, it is beneficial to → **Wear Compression Stockings** to prevent DVT. **HOWEVER**: • If the patient is admitted with [**Acute Stroke**], to prevent DVT, use: → **Intermittent pneumatic compression**. Be careful, **intermittent pneumatic compression** is preferred if the patient is admitted with **acute stroke**! Elastic compression stockings are not beneficial in acute stroke; they are helpful in general surgeries. Both are used to prevent venous thromboembolism. Both were asked before.

Intermittent pneumatic compression

NICE recommends using intermittent pneumatic compression in patients admitted with acute stroke. It is started in the first 3 days of admission and continued until 30 days or until the patient is discharged or started to move. It is not used to treat stroke but to prevent DVT (deep vein thrombosis).

Key 94

Q) Why is it important to receive parenteral vitamin B12 after gastrectomy?

→ Due to loss of intrinsic factors.

Gastrectomy → Loss of the intrinsic factors that are produced from stomach → impaired Vitamin B12 (Cobalamin) absorption → Vitamin B12 deficiency.

Parenteral vitamin B12 = IM Hydroxocobalamin.

	Stomach produces intrinsic factors that help the absorption of vitamin B12 later in small intestine and distal ileum.
Key 95	**In any hemorrhage that causes hemodynamic instability (eg, SBP < 90 mmHg):** • If the question asks about the **INITIAL** step → **IV fluids**. • **After that:** ◙ If it is a **MAJOR bleeding** and the patient is on warfarin: √ Stop warfarin. √ Give **IV** 5 mg vitamin **K1** (to reverse warfarin. Careful: **IV** NOT ORAL)! √ Give prothrombin complex concentrate (**PCC**) (or if unavailable: fresh frozen plasma -FFP-). *If you are to pick between (PCC) and (Vit. K) in the exam, pick → **PCC**. This is because PCC works faster. In reality, we would give both in major bleeding.* ◙ If **INR is > 8** ± **Minor** Bleeding: √ Stop Warfarin. √ Administer IV **or** oral Vitamin K1 (Phytomenadione). √ Restart warfarin when INR < 5.

◙ If **INR 5-8** + **Minor** Bleeding:

√ Stop Warfarin and Check INR the following day.

√ Administer IV or oral **Vitamin K1** (Phytomenadione).

√ Restart warfarin when INR < 5.

(Similar to the above one).

◙ If **INR 5-8** + **NO** Bleeding:

√ Stop Warfarin and Check INR the following day.

√ Restart warfarin when INR < 5.

(Similar to the above one but here no bleeding and so no vitamin K).

So, if the INR between 5 and 8, stop warfarin and restart it when INR is < 5. (This is in all cases). If WITH minor bleeding (eg, epistaxis), give vitamin K. If No bleeding, no need for vitamin K.

◙ If **INR < 5** (but still higher than the target level):

√ Reduce (Or) Omit one or two doses of Warfarin.

√ Measure INR in 2-3 days.

Examples:

	♦ **Major** Bleeding → Intracranial bleeding, GIT bleeding, Internal large vessels bleeding (eg, leaking abdominal aortic aneurysm). ♦ **Minor** Bleeding → Epistaxis, Hematuria.
Key 96	**In patients who are on DOAC (eg, apixaban, rivaroxaban) and going to have surgery:** • If **low** bleeding risk surgery → Stop DOAC **24 hrs** before surgery. • If **high** bleeding risk surgery → Stop DOAC **48 hrs** before surgery. (In most cases, bridging is **not** required with DOACs). Resume the DOAC one day after a low bleeding risk procedure and 2–3 days after a high bleeding risk procedure. Consider daily prophylactic heparin for patients at high risk of venous thrombosis prior to DOAC recommencement.
Key 97	**Important Note:** ▫ If both serum vitamin B12 and Folate are low, we start with treating vitamin B12 deficiency before treating Folate deficiency. ▫ **Mnemonic** → In alphabet: **B** before **F** → treat vitamin **B**12 before **F**olate deficiency.

Key 98

Vitamin B12 Deficiency "*updated*"

Megaloblastic Anemia = low Hb, **high** MCV

→ Either **vitamin B12** deficiency or **Folic acid** deficiency or both.

Vitamin B12 = Cobalamin.

◙ Causes of Vitamin B12 deficiency

- **Pernicious Anemia** (The most common cause).

  Pernicious Anemia → Autoimmune Gastric Atrophy

  → ***Loss of intrinsic factors*** that are required for Vit B12 absorption.

  Usually associated with other autoimmune diseases eg, hypothyroidism.
- **Total Gastrectomy** (Impaired Vit B12 Absorption).
- **Ileal Resection**. (Malabsorption: the majority of vit B12 is absorbed in the terminal ileum)
- **Crohn's Disease**.
- **Chronic Pancreatitis** (malabsorption).
- **Celiac Disease** (malabsorption).
- **Dietary** (Vegans). Remember that Vit B12 is present in **meat**, **fish** and **dairy products** but not in the vegetables. Folic acid is in green vegetables.

Thus, vegans often develop vitamin B12 deficiency.

And, those who do not eat vegetables often develop Folate deficiency.

◙ Features of Vitamin B12 deficiency

- **Peripheral paraesthesia**.
- **Impaired position and vibration** (**proprioception**) **sense**.
- **Dementia** → *loss of memory* + *difficulties with thinking*.
- If untreated → permanent **Ataxia**.

◙ Lab Results of Vitamin B12 deficiency

- **↑ MCV** (usually > 110) + ↓ Hb: Macrocytic Anemia.
- **Hypersegmented Neutrophils on a blood smear**.
- ↑ Homocysteine.

These Lab results are also present in Folic Acid deficiency.

So, How to Differentiate?

By the History:

- **Vegans** (who do not eat meat, fish, dairy products) → Vit B12 deficiency.
- If the patient **does not eat vegetables** → Folic Acid deficiency.
- Gastric or ileal resection → Pernicious Anemia → Vit B12 Deficiency.

◙ Treatment of Vitamin B12 Deficiency

→ **IM Hydroxocobalamin (ie, Vitamin B12 IM injections)**.

Quick Scenario (1):

A man has **low serum folate** → Encourage him to eat **leafy green vegetables**.

Quick Scenario (2):

A man has **low serum folate and low vitamin B12**

→ **Treat vitamin B12 deficiency first (eg, give vitamin B12 injections)**.

(Mnemonic: **B** before **F** → treat vit **B**12 deficiency before **F**olate deficiency)

Quick Scenario (3):

A young man presents with several attacks of pancreatitis. He has peripheral paraesthesia, loss of proprioception in his legs, loss of memory and difficulties with thinking.

Dx→ **Vitamin B12 Deficiency**.

Rx → **Hydroxocobalamin (ie, vitamin B12 IM injections)**.

Key 99

Haematology Case:

Infection (**sepsis**: high temperature, high WBCs, high CPR, high heart rate)

+

Brusing, purpura, bleeding from sites: eg, venepuncture sites, nose (epistaxis)

+

↑ PT, ↑ PTT, ↓ Platelets.

Think → Disseminated Intravascular Coagulopathy (DIC).

Key 100

The sites of the main absorption of:

- **Iron → Duodenum.**
- **Folic Acid (Folate) → Duodenum** and **Jejunum.**
- **Vit B12 → Terminal** (**Distal**) **Ileum.**
- **Bile salts → Terminal** (**Distal**) **Ileum.**
- **The majority of nutrients → Jejunum.**

To make it easy, memorise the following:

Iron → duodenum.

Folate → jejunum (and duodenum).

Vit B12 → Terminal ileum.

Q1) A man with folate deficiency. What is the affected organ (if any)?

→ Duodenum/ jejunum (proximal small intestine) eg, crohn's, celiac.

Q2) Ileal resection (malabsorption) + Fatigue and Palpitation (due to Anemia) + low hemoglobin and High MCV. What is the deficiency?

→ Vitamin B12 deficiency.

Low Hb and high MCV → megaloblastic (vit. B12 OR Folate deficiency).

Ileal resection? Vitamin B12 is absorbed mainly in ileum, while folate is absorbed mainly in duodenum and jejunum. **So** → Vit. B12 deficiency.

Key 101

Quick Revision on Multiple Myeloma:

• The presence of: fatigue, bone pain, recurrent infections, anemia, hypercalcemia (↑Ca^{++}), monoclonal spike on protein electrophoresis suggest multiple myeloma.

• Multiple myeloma is a malignancy of plasma cells.

→ Urgent referral to a haematologist (within 2 weeks).

• in hemato-oncology → confirmation by bone marrow biopsy → Staging of the disease → Initiation of the treatment.

If a multiple myeloma patient presents to the GP with a sudden severe back pain → suspect spinal cord compression → Send immediately to A&E to be seen and evaluated by orthopaedics. Spinal cord compression is serious and could result in neurological damage. A GP would not be able to deal with it.

Key 102	A 58-year-old man underwent a gastric banding 18 months ago presents with lethargy, limb weakness, and paraesthesia of fingers. What to request? A) Bone marrow biopsy. B) Liver function test. C) Renal function test. D) Thyroid function test. E) Haematinics. **Answer → E.** Performing gastrectomy → Reduces the gastric intrinsic factors → Reduces vitamin B12 absorption → Results in Vitamin B12 deficiency → Which can manifest as limb weakness, paraesthesia, and lethargy due to anemia. → Request Haematinics (**Haematinics** = vitamin B12, Iron, Ferritin and Folate).
Key 103	**Scenario**: A 55-year-old man has recently -4 days ago- had intracerebral haemorrhage. Now, he developed DVT in the left leg confirmed by doppler U/S "large thrombus extending from the common femoral vein up into the iliac vein". What is the most appropriate management? → Percutaneous thrombectomy.

	• Note that in a **recent hemorrhagic stroke**, it is contraindicated to give anticoagulants eg, Low molecular weight heparin (LMWH), Direct Oral Anticoagulants (DOAC), Unfractionated heparin, Warfarin.
Key 104	**Quick Points to Remember:** ◙ Sickle cell disease patient + develop chest pain, fever, severe vertebral pain: → Admit for IV fluids, analgesics, and further investigations. Another valid answer → (Refer to hospital for same day review). (Acute sickle cell crisis, potentially complicated by acute chest syndrome even if the chest X-ray is clear. The vertebral pain is mostly due to ischemic crisis seen in sickle cell patients. Remember that sickled RBCs can obstruct vessels in various tissues causing ischemia eg, bone ischemia and infarction). --- ◙ After initiating chemotherapy in a leukemia patient, he develops fatigue, lower back pain, decreased urine output, ↑ serum potassium, and deteriorated renal function test: → The most likely diagnosis → Tumor lysis syndrome (TLS). → request → Urate level. √ Remember: in TLS: ↑ Uric Acid, ↑ K^+, ↑ Phosphate, ↓ Calcium. √ The most specific one of the above → ↑ Urate (uric acid) serum levels.

√ TLS occurs mainly in Leukemia (Especially ALL) and Lymphoma (Particularly Burkitt's Lymphoma) after initiating Chemotherapy.

√ It is a hemato-oncological emergency as it rapidly leads to Renal Failure (High Urea and Creatinine).

√ The management is complicated; however, remember that IV fluid is an important part of the management.

◙ A man presents with 2 months history of fever, night sweats, and unexplained weight loss. He has splenomegaly. He has a history of visiting USA, New York City 2 months ago:

→ Lymphoma (particularly: Non-Hodgkin's lymphoma).

The symptoms resemble that of brucellosis. However, the history of travel to New York City makes brucellosis less likely. Brucellosis develops after a history of consuming unpasteurised dairy products or direct contact with livestock. Brucellosis is extremely rare in urban areas like New York City due to effective public health measures and animal control programs.

◙ A man on apixaban (DOAC) for atrial fibrillation develops intracranial hemorrhage confirmed on CT scan.

→ Prothrombin complex concentrate.

Key 105

An Important Scenario on A Previous Topic

A 58-year-old woman presents to the Emergency Department with severe abdominal pain, bloody diarrhea, and extreme fatigue. She reports that the symptoms began two days ago after returning from a hiking trip. On examination, she is febrile with a temperature of 38.7°C and appears dehydrated.

Investigations:

Hemoglobin: 95 g/L (115-160)

White cell count: 15 x 10^9/L (4-11)

Urea: 20 mmol/L (2.0-7)

Creatinine: 320 µmol/L (70-150)

eGFR: 38 mL/min (>90)

A peripheral blood smear shows the presence of helmet cells. Stool cultures are pending. She consumed undercooked ground beef and untreated stream water during her trip. What is the most likely causative organism?

Options:

A. Norovirus.

B. Campylobacter jejuni.

C. Haemophilus influenzae.

D. Escherichia coli.

E. Rotavirus.

Answer → D. Escherichia coli (EHEC).

Detailed Explanation:

The most likely causative organism in this scenario is Escherichia coli, specifically the enterohemorrhagic E. coli (EHEC) strain. EHEC, also known as Shiga toxin-producing E. coli (STEC), is a common cause of foodborne illness, particularly following the consumption of undercooked ground beef and contaminated water.

Explanation of Kidney Function Deterioration:

The patient's kidney function tests are deteriorated, as evidenced by elevated urea and creatinine levels and a reduced eGFR. This is likely due to the development of hemolytic uremic syndrome (HUS), a complication of EHEC infection. HUS leads to microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury due to the effects of Shiga toxin on the renal microvasculature, causing endothelial damage and resulting in reduced renal perfusion and filtration.

Remember: Eating Undercooked Contaminated food → **E. Coli** O157 → Produce verotoxin → Profuse Diarrhea → Bloody Diarrhea → (after 2-14 days) → Uremia "Acute Renal Failure" (Hematuria, Proteinuria, ↑ Urea and Creatinine).

Mentioning that the blood smear shows "**helmet cells**" or "**schistocytes**" indicates the presence of fragmented red blood cells. These cells are usually seen in conditions where there is mechanical damage to the red blood cells as they circulate through the body. The presence of schistocytes suggests microangiopathic hemolytic anemia (MAHA), which can be associated with

several serious conditions, including Hemolytic Uremic Syndrome (HUS): Often caused by Shiga toxin-producing Escherichia coli (such as E. coli O157).

Here is a detailed explanation of why each option is chosen or not:

A. Norovirus: Norovirus typically causes viral gastroenteritis, presenting with vomiting and non-bloody diarrhea. It is less likely to cause hemolytic anemia or severe kidney dysfunction.

B. Campylobacter jejuni: While Campylobacter can cause gastroenteritis and is associated with consuming undercooked poultry or contaminated water, it is less likely to cause the severe hemolytic anemia and acute kidney injury seen in this patient.

C. Haemophilus influenzae: Haemophilus influenzae is not typically associated with gastroenteritis; it more commonly causes respiratory infections.

D. Escherichia coli (EHEC): This is the correct answer. EHEC/STEC is known to cause severe gastrointestinal symptoms, including bloody diarrhea, and can lead to hemolytic uremic syndrome (HUS). HUS is characterized by the triad of hemolytic anemia, thrombocytopenia, and acute kidney injury, which fits the patient's presentation and lab findings.

E. Rotavirus: Rotavirus primarily affects young children and typically causes non-bloody diarrhea. It is less likely to cause severe systemic symptoms and kidney dysfunction in adults.

Key 106

Differentiating Leukemia Types

Leukemia Type	Typical Age Group	Key Clinical Features
Acute Lymphoblastic Leukemia (ALL)	Children (e.g., Up to 15 Years Old)	- Pancytopenia (a reduction in the number of red blood cells, white blood cells, and platelets). - Presence of immature blast cells in the bone marrow and peripheral blood (*hallmark*).
Acute Myeloid Leukemia (AML)	Adults (Common in two age frames: 20-40 Years Old and Over 60 Years Old)	- Auer rods (needle-like inclusions) present in the cytoplasm of myeloblasts (*characteristic feature*). - Presence of immature blast cells in the bone marrow and peripheral blood (*hallmark*).
Chronic Myeloid Leukemia (CML)	Middle Age (40-50 Years Old), but can occur in younger or older adults	- Massive splenomegaly (*characteristic feature*, especially in later stages). - Presence of the Philadelphia chromosome (BCR-ABL fusion gene) (*hallmark*). - Increased number of mature granulocytes (neutrophils, basophils, eosinophils) without blast cells. - Cells in all stages of maturation (e.g., myelocytes, metamyelocytes, etc.).
Chronic Lymphocytic Leukemia (CLL)	Older Adults (Over 60 Years Old)	- Typically, no or mild splenomegaly. - Presence of smudge cells (fragile lymphocytes) in the blood smear (*characteristic* feature). - Cervical lymphadenopathy (enlarged lymph nodes in the neck). - Presence of mature lymphocytes (*hallmark*).

Key 107

A Scenario on A Previous Topic

A 55-year-old man presents to his GP with a 2-month history of fatigue and night sweats. On physical examination, his spleen is found to be significantly enlarged, extending 10 cm below the costal margin. There is no lymphadenopathy. Blood tests show a significantly raised white blood cell count. What is the most likely cell type that would be observed on a blood smear?

A) Blast cells.

B) Target cells.

C) Helmet-shaped cells.

D) Sickle cells.

E) Predominance of mature granulocytes.

The correct answer is → **E) Predominance of mature granulocytes**.

Here's why:

• This presentation is highly suggestive of **chronic myeloid leukaemia (CML)**, which typically occurs in middle-aged to older adults.

• The patient's symptoms of fatigue, night sweats, and massive splenomegaly, combined with a markedly elevated white blood cell count, point towards CML.

• In CML, the **blood smear** characteristically shows a predominance of **mature granulocytes**, including neutrophils, basophils, and eosinophils, along with their precursors.

Other options:

A) **Blast cells**: These are immature cells typically associated with acute leukaemias. In CML, blast cells are usually less prominent unless the disease has progressed to a blast crisis, which is a more advanced stage.

B) **Target cells**: These are red blood cells with a bullseye appearance, commonly seen in conditions like thalassaemia or liver disease. They are not associated with elevated white blood cell counts.

C) **Helmet-shaped cells**: These cells, also known as schistocytes, are fragmented red blood cells seen in conditions like haemolytic anaemia or microangiopathic processes. They are not typically associated with leukaemia.

D) **Sickle cells**: These abnormal, crescent-shaped red blood cells are seen in sickle cell disease, a haemoglobinopathy. They do not present with a raised white blood cell count or splenomegaly of this magnitude.

In summary, the patient's clinical picture is most consistent with **chronic myeloid leukaemia**, where a **predominance of mature granulocytes** would be expected on a blood smear.

Important:

- **Acute Lymphoblastic Leukaemia (ALL)**:

Characterised by **pancytopenia** (reduced red and white blood cells, platelets) and the **presence of immature blast cells** in both the bone marrow and peripheral blood.

- **Acute Myeloid Leukaemia (AML)**:

Notable for **Auer rods** in the cytoplasm of myeloblasts and the **presence of immature blast cells** in the bone marrow and peripheral blood.

- **Chronic Myeloid Leukaemia (CML)**:

	Features include **massive splenomegaly**, the **Philadelphia chromosome (BCR-ABL fusion gene)**, and an **increased number of mature granulocytes**. Cells at various stages of maturation are also present. • **Chronic Lymphocytic Leukaemia (CLL)**: Identified by **smudge cells** in the blood smear, **cervical lymphadenopathy**, and the **presence of mature lymphocytes**, with typically no or mild splenomegaly.
Key 108	A Scenario on A Previous Topic A 25-year-old female arrives at the Emergency Department with a 6-day history of worsening fatigue. She also complains of persistent, watery diarrhoea that started 5 days ago. Over the last 48 hours, she has not passed any urine. Upon examination, she is lethargic, has generalised oedema, and her blood pressure is 135/85 mmHg. Her heart rate is 88 beats per minute, and her respiratory rate is 18 breaths per minute. Her abdomen is soft with normal bowel sounds. Investigations: Haemoglobin: 65 g/L (115-160) Platelets: 95 x 10^9/L (150-400)

Potassium: 6.2 mmol/L (3.5-5)

Urea: 22 mmol/L (2.0-7.0)

Creatinine: 320 µmol/L (70-150)

eGFR: 10 mL/min (>90)

What would be the most appropriate next step in her management?

A) Blood transfusion.

B) Co-amoxiclav.

C) Dialysis.

D) Intravenous fluids.

E) Platelet transfusion.

Answer:

• The patient's presentation suggests **haemolytic uraemic syndrome (HUS)**, which is often secondary to a gastrointestinal infection, commonly associated

with **Shiga toxin-producing Escherichia coli**. The classic triad of HUS includes **microangiopathic haemolytic anaemia**, **thrombocytopenia**, and **acute kidney injury (AKI)**.

• Given the patient's elevated **potassium level (6.2 mmol/L)** and evidence of **acute kidney injury**, the most urgent and life-threatening issue to address is **hyperkalaemia**.

• **Dialysis** is the most appropriate step to manage both **the renal failure** and the **dangerously high potassium level**.

Summary of Key Considerations:

- **Hyperkalaemia** is life-threatening, especially at levels ≥6 mmol/L, and needs immediate intervention to prevent fatal arrhythmias.
- **Dialysis** is indicated in severe AKI (acute kidney injury) with hyperkalaemia, as it can efficiently remove excess potassium and manage fluid overload.
- **Packed red cell transfusion** (blood transfusion) may worsen hyperkalaemia since stored blood contains potassium, which could exacerbate the patient's condition.
- **Intravenous fluids** are considered if there is a volume depletion cause of AKI, but in this case, the patient shows signs of fluid overload.

- **Platelet transfusion** is unnecessary unless there is active bleeding or a significantly lower platelet count (e.g., <10 x 10^9/L).
- **Antibiotics** (such as Co-amoxiclav) are not indicated here, as antibiotic use in HUS related to diarrhoeal illness can worsen the condition.

Thus, the correct answer is → **C) Dialysis**.

Additional Information (Reading):

Types of Dialysis:

√ Dialysis is A medical procedure that removes waste and excess fluid from the blood when the kidneys cannot function properly.

√ Hemodialysis is the more common type of dialysis worldwide.

◙ **Hemodialysis**:

- Blood is taken from the body, filtered through a machine (dialyser), and returned to the body.
- Requires a vascular access point (like a fistula or catheter).
- Typically performed in a hospital or dialysis centre.

	• **Most common indications**: Chronic kidney disease (CKD), acute kidney injury (AKI) with severe electrolyte imbalances (e.g., hyperkalaemia), fluid overload, and uremia (build-up of waste products in the blood). ◙ **Peritoneal Dialysis**: • Uses the lining of the abdomen (the peritoneum) to filter the blood. • A special fluid is placed in the abdomen, absorbs waste, and is then drained out. • Can be done at home, offering more flexibility. • **Most common indications**: CKD in patients who prefer home treatment, those unable to tolerate hemodialysis, or in certain cases of AKI.